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MENTAL RETARDATION ABSTRACTS

Volume 10 Number 3 July-September 1973

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compiled by Nancy Jarvis and Edward Leyman

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BROAD ASPECTS OF MENTAL RETARDATION

1688 **GLASS, BENTLEY.** Human heredity and ethical problems. *Perspectives in Biology and Medicine*, 15(2):237-253, 1972.

The discovery of the chemical basis of heredity during the last 20 years has greatly extended man's power over nature, with a concomitant extension of his responsibility. "Euphenics," modification of defective phenotypes by genetic techniques, now competes with eugenics in efforts to produce a disease free population. Identification of inborn metabolic errors such as phenylketonuria or galactosemia, and the development of chromosome karyotyping and amniocentesis, suggest the possibilities of limiting the right to reproduce in cases of genetic disease, therapeutic abortion, or sterilization, all of which present ethical problems. Genetic control is complex because many genes express themselves only after long delay; others, because of environmental effects, may not be expressed at all, although they may be transmitted. Multifactorial inheritance may be modified environmentally to prevent expression of overt disease, but such modification itself may produce a dysgenic increase in the frequency of detrimental genes. Some genes are detrimental in one environment but favorable in another; some heterozygous genes are more favorable than either of the homozygous types. Genetic engineering techniques raise formidable ethical, legal, and social questions that must be answered if we are not to make genetic decisions by default. Cloning, sperm banks, and embryo implants may make possible the breeding of a "good race," if such could be defined, but selection for some optimum characteristics seems to involve the sacrifice of others. Does society, which bears the cost of genetic misfortune, have the right to protect itself from such misfortune? What will be the effect of the complete liberation of the sexual life from its relationship to reproduction? Such questions, which illustrate the value crisis induced by genetic technology, require the attention of the wisest men of our times. (6 refs.) - *N. Jarvis*.

State University of New York
Stony Brook, New York 11790

1689 **FLETCHER, ANNE B.; MILHORAT, THOMAS H.; RANDOLPH, JUDSON G.; ENG, GLORIA D.; STRAIGHT, BELINDA; & D'AGOSTINO, ANGELO D.** The right to life and the right to die with dignity. *Clinical Proceedings, Children's Hospital National Medical Center*, 28(9):233-250, 1972.

Increasing refinements of medical technology have made it possible to maintain severely defective patients in life, thus raising so many questions about the quality of that life as to require a thorough reconsideration of the problems a defective birth entails. A conference held at the Grand Rounds, Children's Hospital National Medical Center, focused on the problems surrounding a child with a ruptured meningomyelocele. Although it was decided that the child should receive only supportive care because of poor prognosis, his condition improved and the meningomyelocele healed spontaneously. Formerly 80% of such patients died within two years; following adoption of the Sheffield Plan of repairing all meningomyeloceles after birth, survival is increased but many have multiple deformities and only 20% can be expected to be intellectually competitive. In Children's Hospital such patients, if they do not have contraindications (paraplegia, severe hydrocephalus, and multiple organ anomalies), undergo ventriculoperitoneal shunting, to be followed later by ventriculoatrial shunting. Children who survive beyond 2-4 years must be evaluated for a possible ileal conduit or a sigmoid colostomy in adolescence. Parents confronted with such an infant may be advised not to have surgery performed, and to "let nature take its course." Among the principles operative in an ethical consideration are distinctions between ordinary and extraordinary means, positive and negative euthanasia, and the question of the parents vs. society as the ultimate authority for decision. Participants in the conference agreed that each case requires its own decision, based upon medical criteria. The suggestion that boards be established to decide on such cases was resisted on the grounds that the physician cannot transfer his responsibility to a group. Some participants suggested that catastrophic medical insur-

ance should be made available in federal plans. If the parents decide that the child should be saved, they must be capable of informed consent to the necessary operations. Dr. Parrott's editorial note appended to the proceedings rejects positive euthanasia and withdrawal of food and drink from inoperable cases, as well as the withholding of simple surgery to facilitate a natural function. (3 refs.) - *N. Jarvis*.

1690 U.S. National Institutes of Health, National Institute of Neurological Diseases and Stroke. Bibliography--the collaborative study on cerebral palsy, mental retardation, and other neurological and sensory disorders of infancy and childhood. (Annual Bibliographies of the Collaborative Perinatal Research Project, Number 4, July 1970 through June 1971.) Bethesda, Maryland, NIH,1972, 22 p.

A compilation of 82 Collaborative Perinatal Research Project publications from July 1970 through June 1971 is provided. Subjects range from abortion and drug addiction in pregnancy to asphyxia, Down's syndrome, fetal viruses, MR, socioeconomic factors and infant development, and child development. - *B. J. Grylack*.

National Institute of Neurological
Diseases and Stroke
Bethesda, Maryland

1691 **MARSTON, ROBERT Q.** Research on minors, prisoners and the mentally ill. *New England Journal of Medicine*, 288(3):158-159, 1973.

The protection of human Ss involved in medical research as outlined by the National Institutes of Health (NIH) is discussed. The policy of these institutes is egalitarian, marking no distinctions of race, color, or socioeconomic status; but it touches only lightly on Ss with limited civil freedom including prisoners, mentally ill patients, and minors. Medical research frequently requires that a convenient stable S population be followed over a lengthy period (weeks or months), so that such available populations as hospitalized patients, inst patients, medical students, and prisoners are often used as Ss. The NIH has reviewed its policy regarding: responsibilities of the grantee; financial compensation to Ss, which should not constitute an undue inducement but be adequate in relation to other services; the condition or terms of the S's confinement as they relate to the research study; and, in the case of the mentally ill, the potential benefits to be derived from participation in such studies for these particular Ss. Special attention will be given to the requirement for informed consent. Immediate attention is now being focused on the protection of human experimental Ss, without waiting for further discussion in committes. - *A. C. Schenker*.

1692 **INGELFINGER, F. J.** Ethics of experiments on children. *New England Journal of Medicine*, 288(15):791-792, 1973.

Ethics with respect to experiments on human Ss are discussed, with particular reference to the studies conducted at Willowbrook State School for MR children. Since the policy of the *New England Journal of Medicine* is against acceptance of investigations performed unethically, the appearance of the Willowbrook report is defended for several reasons. If the statement of the World Medical Association regarding subjecting a human being to a procedure other than in the interest of the patient is taken literally, Ss who are incapable of giving informed consent, such as young children and the mentally incompetent, are categorically excluded from all investigations except those that may benefit them directly. Other journals contain accounts of experiments in children; in each of these, the risk to the S is extremely small. The World Medical Association's declaration is neither observed nor practical and should be modified. Perhaps some golden mean can be established in connection with such experiments that would satisfy society as a whole. (8 refs.) - *A. C. Schenker*.

1693 **FOX, RICHARD.** Aspects of handicap *Lancet*, 1(7760):1113-1114, 1972.

Two recent British films, "A Day in the Death of Joe Egg" and "Like Other People," contribute much to the maturing of a human and realistic understanding of mental and physical disability. Unlike most previous attempts to convey a sense of the essential humanity of handicapped people -- as well as to look honestly at the tragic aspects of their situation -- both films suggest profound social implications and yet manage to avoid the special pleading and caricaturing typical of earlier cinematic efforts. The first film looks at the

birth of a severely handicapped child and its effect on the young parents' marriage, while the second focuses on the development of a love relationship between two adults with severe physical handicaps. (4 refs.) - *N. Mize*.

1694 **NIXON, ROBERT K.** Ethical principles in human experimentation. *New England Journal of Medicine*, 288(23):1247, 1973. (Letter)

Referring to an article by Dr. Malcolm Watts on a new ethic for medicine and society, Franz Ingelfinger applies this ethic in defense of experiments on children. Dr. Ingelfinger suggests that society has a right to use children and the mentally incompetent for experimentation provided the risks are judged to be small. Justifying the use of children on this basis allows for the inevitable extension to the MR and in turn to other undesirable groups of our society. Although human experimentation is of great value to society, it should be conducted in a setting of informed consent and not at the price of an individual's freedom. - *A. C. Schenker*.

Henry Ford Hospital
Detroit, Michigan

1695 **CALLIE, ALBERT S.** Ethical principles in human experimentation. *New England Journal of Medicine*, 288(23):1247, 1973. (Letter)

The editorial on the ethics of experiments on children is criticized from the viewpoint that, whereas the author considers the rights of society, he does not consider the rights of the children or mentally incompetent persons. It is necessary that a reverence for life be developed to such extent that experimentation on anyone that is not primarily designed for the benefit of that individual can be dismissed from our minds. It is submitted that we should try to benefit society as a whole, as well as the individual, whether a child, a mentally incompetent person, or even one who is an unborn child. The two concepts, one of helping the individual and the other of helping society, are not contradictory. - *A. C. Schenker*.

Tucson Clinic
Tucson, Arizona

1696 **BAUMSLAG, NAOMI; & YODAIKEN, RALPH E.** Ethical principles in human experimentation. *New England Journal of Medicine*, 288(23):1247, 1973. (Letter)

The opinion is expressed that there are no conditions under which children may be used for experimentation not primarily designed for their benefit. The Willowbrook experiments are considered immoral and ethically indefensible. Although informed consent was obtained by involved parent group discussions, many of the social pressures may have operated, even with the conscious knowledge of the investigators. Physicians, although well motivated, tend to believe in their omniscience and omnipotence. The Hippocratic oath is recalled with respect to a promise not to cause hurt or prejudice to the patient. (4 refs.) - *A. C. Schenker*.

Emory University
Atlanta, Georgia

1697 **HUSKINS, DENNIS G.** Ethical principles in human experimentation. *New England Journal of Medicine*, 288(23):1247-1248, 1973. (Letter)

The opinion is expressed that it was wrong to use the MR children of the Willowbrook State School in Staten Island for experiments that exposed them to parenteral live serum B hepatitis. The article never mentioned the topic of consent. Why were these MR children used? Have the remote risks of subacute hepatic necrosis, of chronic active hepatitis, or of death been considered? Medical experimentation on MR children that entails any degree of morbid risk is immoral. - *A. C. Schenker*.

St. Lukes Hospital Center
New York, New York

1698 **SZUL, MICHAEL.** Ethical principles in human experimentation. *New England Journal of Medicine*, 288(23):1248, 1973. (Letter)

Experimentation on mentally deficient and inst children is deplored. The research conducted by Dr. Krugman strips the children of the dignity afforded to fully functioning human beings. Physicians who, after identifying their weaker fellow humans, do not protect them but exploit them, are to be censured. A society that con-

dones such procedures is an unhealthy one. - *A. C. Schenker.*

University of Manitoba
Winnipeg, Manitoba, Canada

1699 **SHINE, IAN; HOWIESON, JOHN; & GRIFFEN, WARD O.** Ethical principles in human experimentation. *New England Journal of Medicine*, 288(23):1248, 1973. (Letter)

Attention is drawn to a modification of the World Medical Association's statement on human experimentation as proposed by Dr. Ingelfinger. This author condones human experimentation when the risks are small and justifiable; this might be acceptable if the experimentor himself would be willing to act as a subject for experiments, or to offer a spouse or child when appropriate. - *A. C. Schenker.*

Thomas Hunt Morgan Institute of Genetics
Lexington, Kentucky

1700 **MALOVANY, ROBERT J.; ROSEN, ORA; MESSENGER, ELI; HARRISON, SUE; WAYNE, PETER; GREEN, LINDA; WALD, BART; & COHEN, JON.** Human rights and research. *New England Journal of Medicine*, 288(24):1305, 1973. (Letter)

Reference is made to Marston's editorial concerning research on human Ss. Criticism is directed at the motivation for trying to protect human Ss, according to Dr. Marston, who appears to be excessively concerned with the status of professionals. It is maintained that true professionalism carries with it the obligation to protect human rights and human welfare. It is no accident that medical research is performed so frequently on Ss who have limited economic and civil freedom; and it is unconscionable that our government is willing to finance research involving human Ss, but is unwilling to fund basic adequate health care for the same people. Physicians who engage in research on Ss who are receiving substandard health care have an obligation to eliminate the exploitation of their patients. - *A. C. Schenker.*

Montefiore Hospital Medical Center
New York, New York

1701 **U.S. PUBLIC HEALTH SERVICE.** *Bibliography: The Collaborative Study on Cerebral Palsy, Mental Retardation, and Other Neurological and Sensory Disorders of Infancy and Childhood. No. 5, July 1971 through June 1972.* (National Institutes of Health, National Institute of Neurological Diseases and Stroke.) Washington, D. C., U.S. Health, Education, and Welfare Department, 1973, 18 p.

This fifth annual bibliography of the Collaborative Perinatal Project of the National Institute of Neurological Diseases and Stroke contains 62 entries, consisting of 12 core data publications of the Perinatal Research Branch, 30 core data publications of collaborating institutions, 5 noncore data publications of the Perinatal Research Branch, and 15 noncore data publications of the collaborating institutions. A subject index by title and an author index are included. - *C. Wares.*

National Institutes of Health
Bethesda, Maryland 20014

1702 **INGELFINGER, F. J.** Informed (but uneducated) consent. *New England Journal of Medicine*, 287(9):465-466, 1972. (Editorial)

The experimental human subject may not fully understand the experiment, or may not have complete freedom of choice. The comprehension of medical information by laymen usually varies inversely with the detail presented, and the Ss' understanding of the impact of the procedures is likely to be deficient. Volunteers are influenced by the hope of reward, but the patient is placed under different pressures of greater severity. The main virtue of the U. S. consent procedures is that the subject understands that the proposed treatment is experimental. The real protection of the patient is the conscience and compassion of the investigator rather than the legal device of "informed consent." (3 refs.) - *V. J. Goldberg.*

10 Shattuck Street
Boston, Mass.

1703 **HOLDEN, CONSTANCE.** World ethics body proposed. *Science*, 177(4045):1174, 1972.

A United Nations group concerned with medical sciences has proposed the creation of an interna-

tional, nongovernmental commission to explore the moral and social issues raised by new and future developments in biology and medicine. The Council for International Organizations of Medical Sciences (CIOMS) had passed this resolution earlier. The proposed body would constitute a step towards recognizing and coping with urgent ethical problems on an international basis. The commission would set up priorities in biomedical research and might encourage governments to sponsor similar efforts on a national basis. - *B. J. Grylack.*

MEDICAL ASPECTS—Diagnosis (General)

1704 **HAINES, J.; & SAINSBURY, P.** Ultrasound system for measuring patients' activity and disorders of movement. *Lancet*, 2(7781):802-803, 1972.

An ultrasound system that has been developed to measure patients' involuntary movements is a valuable method with numerous applications to clinical research. An attempt to utilize the method to confirm an obvious cultural difference in use of gesture between French and English students corroborated the sensitivity and practicability of the system. (1 ref.) - *B. J. Grylack.*

Graylingwell Hospital
Chichester, Sussex, England

1705 **PEARSON, PETER.** The use of new staining techniques for human chromosome identification. *Journal of Medical Genetics*, 9(3):264-275, 1972.

Review of developments in new staining techniques for human chromosome identification over the past two years indicates the practical superiority of these techniques over morphological identification. The fluorescent technique can be used for sexing cells and provides for observation of both intensely fluorescent areas and chromosome bands on the same chromosome preparation. Moreover, this technique does not appear to suffer from the variation in quality characteristic of other methods. However, if the Giemsa banding techniques are modified to achieve a higher level of reliability, they are preferable to the quinacrine fluorescence, since they require ordinary bright field microscopes and employ permanent preparations. (93 refs.) - *B. J. Grylack.*

Leiden University
The Netherlands

1706 **MACEK, MILAN; REZACOVA, DAGMAR; & KOTASEK, ALFRED.** Simple smear technique for the sampling and culturing of embryonal and fetal tissues. *Humangenetik*, 16(3):245-249, 1972.

Tissue cultures were prepared from skin, amnion, umbilical cord and amniotic fluid of 6 16-24-wk-old fetuses and the skin of 8 8-10-wk-old embryos. Samples were taken with sterile monofil meshes which were used to smear the surface of the tissue; the meshes were placed directly into the culture medium. Skin smears from fetuses were successful in 5/6 cases and subculturing was possible at the end of the third week; umbilical cord samples were successful in only 1/5. The skin cultures of embryos were successful in all cases and growth was rapid. The monofil mesh provides a gentle means of sampling of fetal skin for prenatal diagnosis and provides culture material with higher growth rates than amniotic fluid. (13 refs.) - *V. J. Goldberg.*

Institute for Child Development
Research
Prague, Czechoslovakia

1707 **FLAMME, P.; & LARDINOIS, C.** Effect of ultrasound. *British Medical Journal*, 3(5837):428, 1972. (Letter)

Although it is often stated that the sound intensity of pulsed ultrasound in diagnostic procedures amounts to a level 500 to 1,000 times weaker than that used in therapy, the intensity of a pulsed dose is the average of the intensities of each of the wave-trains, and the mechanical effects of pressure and acceleration that result may be serious. It is disquieting to think of the effect of diagnostic ultrasound on the fetus in utero and in particular on weaker structures such as the mitochondria. (2 refs.) - *B. J. Grylack.*

Hopital Saint-Georges
Mons, Belgium

1708 **TIPTON, R. H.** Continuous fetal heart rate. *British Medical Journal*, 1(5797):439-440, 1972. (Letter)

The lead article on continuous fetal heart rate in a previous issue of *British Medical Journal* is misleading in its use of terminology and its reporting of research. "Fetal hypoxia" is more accurate than "fetal asphyxia." Hon did not show that early decelerations are associated with cord compression but rather described type I dips as due to head compression and type O dips as due to cord compression. Dip area is not primarily a measure of amplitude of dips but a measure of duration, frequency, and amplitude. Fetal scalp sampling is a valuable method of assessment of fetal status, but interpretation of fetal pH is difficult. At present, fetal heart rate monitoring in labor is the method of choice since it is continuous. (11 refs.) - *B. J. Grylack*.

Jessop Hospital for Women
Sheffield, Yorks, England

1709 **SCHLUETER, MUREEN A.; JOHNSON, BARBARA B.; SUDMAN, DOROTHY A.; WANG, LESLIE Y.; NAMKUNG, PAULETTE; HEASLEY, SUZANNE V.; HADDOCK, SUSAN A.; & TOOLEY, WILLIAM H.** Blood sampling from scalp arteries in infants. *Pediatrics*, 51(1):120-122, 1973.

With the use of a modification of a technique for intermittent sampling of arterial blood from the temporal artery of small infants, scalp arterial puncture has been performed successfully during the past 6 and a half years for obtaining repeated samples of arterial blood. Few complications have been encountered, even in the preterm infant. Scalp arterial puncture is especially valuable in the management of the preterm infant who requires prolonged oxygen therapy. (4 refs.) - *B. J. Grylack*.

Cardiovascular Research Institute
University of California
San Francisco, California 94122

1710 **CAMPBELL, STUART; & KURJAK, ASIM.** Comparison between urinary oestrogen assay and serial ultrasonic cephalometry in assessment of fetal growth retardation. *British Medical Journal*, 3(5836):336-340, 1972.

A total of 284 patients, 87 (31%) of whom were small for dates and 46 (17%) had a low Apgar score, were assessed by urinary estrogen assay and serial ultrasonic cephalometry because of possible risk to the fetus from fetal growth retardation. Of the 284 cases, there were 14 perinatal deaths (5.1%) and 8 gross fetal abnormalities (2.8%). Of 97 cases where the predictions based upon the ultrasonic and estrogen results disagreed, 28 of 37 small-for-dates babies were in the retarded ultrasonic growth groups, while only 9 were in the 2+ abnormal estrogen group. A significantly higher number of these babies was categorized correctly by ultrasonic cephalometry ($\chi^2 = 8.48$, $p<0.005$). In contrast, there was no significant difference in the distribution of normal and low Apgar scores between the 2 methods ($p>0.9$). Five of the 14 stillbirths were in the normal estrogen group, and 3 were in the normal ultrasonic growth category. Ultrasonic cephalometry, which gives earlier warning of impaired placental function than does estrogen excretion, was distinctly superior to urinary estrogens in predicting fetal growth retardation, although it did not show an advantage in the prediction of perinatal asphyxia. (24 refs.) - *B. J. Grylack*.

Institute of Obstetrics and
Gynaecology
Queen Charlotte's Maternity Hospital
London W.6, England

1711 **WU, KENNETH KUN-YU; JACOBSEN, CARL D.; & *HOAK, JOHN C.** Plasminogen in normal and abnormal human cerebrospinal fluid. *Archives of Neurology*, 28(1):64-66, 1973.

Plasminogen concentrations in the cerebrospinal fluid (CSF) of patients with various neurological disorders were determined and correlated with protein concentrations. The CSF samples were collected from 63 adult patients, 14 of whom had medical disorders without neurological involvement (arteriosclerosis, psychoneurotic disturbances, chronic renal failure, acute leukemia, and upper respiratory infection); the 49 with neurological diseases included: cerebral thrombosis, cerebral hemorrhage, cerebral neoplasm, pyogenic meningitis, multiple sclerosis, idiopathic polyneuritis, epilepsy, presenile dementia, postmenopausal myopathy, cervical spondylosis, intervertebral disc herniation, alcohol encephalopathy, trigeminal neuralgia, Friedreich's ataxia, and hydrocephalus. Trace amounts of plasminogen

were found in 5 of the medical disorders. The highest values occurred in the acute stage of pyogenic meningitis. There was close correlation between the plasminogen and protein concentrations in the CSF from all the patients. This finding suggests that the CSF plasminogen is probably derived from the blood, rather than produced within the nervous system. (3 refs.) - *A. C. Schenker.*

*University of Iowa Hospitals
Iowa City, Iowa, 52240

1712 **GREENAWALD, K. A.; SPEICHER, C. E.; EVERS, W.; & *HENRY, J. B.** Glucose content in cerebrospinal fluid: a comparison with glucose levels in serum as determined by copper reduction and hexokinase methods. *American Journal of Clinical Pathology*, 59(4):518-520, 1973.

The relationship of glucose content in serum to that in cerebrospinal fluid was evaluated in 29 patients, using a more specific method for glucose determination than has been generally used. Glucose was measured by an automated neocuproine method with the Technicon Auto-Analyzer II, and by an automated hexokinase method using the DuPont Automatic Clinical Analyzer (ACA). The data indicated that although there was a great overlap in the normal ranges, the CSF glucose values in normal fasting patients were significantly lower ($p<0.01$) with the hexokinase than with the copper reduction method. This is probably due to nonspecific reducing substances in the sera crossing the blood-brain barrier; this is corroborated by the similar CSF:serum glucose ratios by the two methods (0.705, 0.712). It is submitted that the hexokinase method, being more specific for glucose, be used for measuring this constituent in CSF. (3 refs.) - *A. C. Schenker.*

Upstate Medical Center
State University of New York
Syracuse, New York 13210

1713 **HSU, LILLIAN Y. F.; STRAUSS, LOTTE; DUBIN, ELYSE; & HIRSCHHORN, KURT.** Prenatal diagnosis of trisomy 18: pathologic findings in 20-week conceptus. *American Journal of Diseases of Children*, 125(2):290-292, 1973.

Progress in the techniques of amniocentesis and cultivation of amniotic fluid cells have advanced prenatal cytogenetic studies to a new level in genetic counseling, enabling the recommendation of therapeutic abortions of fetuses known to have major chromosomal abnormality. Such prenatal studies were performed on the 16.5-week fetus of a 40-yr-old multipara. A diagnosis of trisomy 18 was made, based on chromosome analysis of the amniotic fluid sample. The fetus was aborted in the twentieth week and was found to have recognizable phenotypic stigmata of trisomy 18, including both external and internal anomalies and growth retardation. External anomalies were apparent in abnormalities of the facies, ears, hands, and neck. Internal anomalies included ventricular and atrial (ostium II) septal defects, bicuspid aortic valve, abnormal configuration of liver, umbilical hernia, Meckel diverticulum, intestinal malrotation, hemivertebrae, and partial absence of the cerebral falx. Pathologic examination of the placenta also disclosed numerous deficiencies. The phenotype of trisomy 18 is well established by midgestation, and may operate progressively throughout development, permitting recognition of the syndrome at various stages of intrauterine life by means of advanced prenatal cytogenetic diagnosis. (14 refs.) - *C. Wares.*

Mount Sinai School of Medicine
New York, N.Y. 10029

1714 **GARLINGER, PATRICIA; HECHT, FREDERICK; PRESCOTT, GERALD H.; WYANDT, HERMAN E.; TOLBY, BLAINE E.; MILBECK, ROSEMARY L.; & OVERTON, KATHLEEN.** Restrictive consent and amniocentesis. *New England Journal of Medicine*, 288(19):1028, 1973. (Letter)

Disagreement is voiced with the notion that, in the performance of amniocentesis, the parents must make a decision regarding termination of pregnancy before the procedure is carried out. The objection is based on a reluctance to withhold a medical procedure from a patient who seeks further information in order to make a crucial decision, and on the restriction that if abortion is not acceptable (under certain conditions) that no amniocentesis will be performed, since this attitude forces the physician's beliefs on the family. Those people who are willing to undertake the rearing of an abnormal child should be given the opportunity of preparing for such event by means of amniocentesis. It is furthermore evident that a private patient may seek this procedure

through other channels than his own physician, whereas the clinic patient must abide by the ruling of the institution. (6 refs.) - *A. C. Schenker.*

University of Oregon Medical School
Portland, Oregon

1715 **HYMAN, CHARLES J.; DEPP, RICHARD; PAKRAVAN, PARVIN; STINSON, DORA A.; & ALLEN, ALEXANDER C.** Pneumothorax complicating amniocentesis. *Obstetrics and Gynecology*, 41(1):43-46, 1973.

A complication of amniocentesis associated with penetration of the fetal thorax is presented. This occurred in a 36-yr-old woman who was admitted to hospital during the forty-first week of her fourth pregnancy, 2 hours after the onset of labor. Five hours after admission, amniocentesis was performed to determine the presence of meconium and the high-risk nature of the labor before administration of Pitocin. The infant was born 4 hours later, was seemingly normal at birth, but revealed petechiae on the left chest wall at 2 hours of age. Subcutaneous emphysema of the left thoracic wall and ipsilateral pneumothorax were revealed in chest films. However, the baby's tachypnea spontaneously resolved, and she recovered subsequently. The amniocentesis needle apparently penetrated the baby's thorax, but the mechanism by which air entered the thorax is not clear. It is recommended that any infant who delivers within several days of amniocentesis should be critically examined for needle marks and crepitus. (20 refs.) - *A. C. Schenker.*

Magee-Womens Hospital
Pittsburgh, Pennsylvania 15213

1716 **MARTIN, CHESTER B., JR.; MURATA, YUJI; & RABIN, LAURA S.** Diagnostic ultrasound in obstetrics and gynecology: experience on a large clinical service. *Obstetrics and Gynecology*, 41(3):379-386, 1973.

Ultrasonic scanning for diagnostic purposes is described as applied in an obstetrics and gynecology service during the first 2 years of its use. A 2-MHz probe using a Kretz Technik 4100 MG/S Scanner was found to be most satisfactory. In all, 1,247 examinations on 854 patients were done during the 25-month period; the greatest increases since the initiation of this technique occurred in scans for fetal measurement and pelvic mass. Placental localization in late pregnancy bleeding was the area of greatest interest; placenta previa was predicted or excluded correctly in 93.4% of the 167 patients for whom delivery information is known. Measurement of the fetal biparietal diameter was carried out to confirm clinical estimates of gestational age in cases of repeat cesarean section. Suspected molar pregnancy was the reason for scanning 38 patients. The technique is considered a simple one and is recommended as an aid to diagnosis, not only in obstetrics and gynecology but in other services as well; indications for such scans include cardiac valvular disease, brain lesions, liver, renal and pancreatic masses, enlarged spleen, and mammary cyst. (19 refs.) - *A. C. Schenker.*

LAC/USC Medical Center
Los Angeles, California 90033

1717 **MERMUT, SAIM; KATAYAMA, K. PAUL; DEL CASTILLO, RENE; & JONES, HOWARD W.** The effect of ultrasound on human chromosomes in vitro. *Obstetrics and Gynecology*, 41(1):4-6, 1973.

The effects of long-term exposure of human chromosomes to ultrasound were studied *in vitro*. Four cultures of fetal umbilical cord blood and 2 cultures of human adult lymphocytes were examined for chromosome damage after exposure to ultrasound; 463 cells were examined after 72-90 hours of such exposure. The examination revealed 8 cells with chromatid breaks, 31 chromatid gaps, and 3 cells with abnormal chromosomes. In a control group of 463 cells, 7 had chromatid breaks, 30 had chromatid gaps, and 1 had an abnormal chromosome. In this *in vitro* model, diagnostic ultrasound does not seem hazardous to chromosomes. (5 refs.) - *A. C. Schenker.*

The Johns Hopkins Hospital
Baltimore, Maryland 21205

1718 **RAINE, D. N.** Special handicaps: biochemical disorders. In: Griffiths, Margaret I., ed. *The Young Retarded Child: Medical Aspects of Care*. Baltimore, Maryland, Williams & Wilkins, 1973, Chapter 14, p. 154-163.

Biochemical tests in the investigation of a mentally abnormal child are numerous and complex. Simple

side room tests of urine may discover cases of phenylketonuria, argininosuccinic aciduria, Lowe's syndrome, galactosemia, gargoylism, Lignac-Fanconi syndrome, and homocystinuria. Grouped laboratory investigations, or screening, of high risk Ss may include both urine and blood tests. Feces and sweat may also be analyzed in this process. Specialized analyses and definitive diagnosis of metabolic disorders associated with mental subnormality depend on the final level on specific tests peculiar to the disease(s) suspected. The most sophisticated general approach so far developed for these final analyses is gas-liquid chromatography combined with mass spectrometry. Management of metabolic disease in the mentally subnormal may or may not include treatment, depending upon the diagnosis and prognosis. The present most common form of treatment of inherited metabolic diseases is some form of dietary restriction. Experimental therapy may yield new and more effective forms of treatment for those biochemical diseases which do not respond to diet therapy. - *C. Wares.*

United Birmingham Hospitals
Birmingham, England

1719 **INSLEY, J.** Special handicaps: malformation syndromes. In: Griffiths, Margaret I., ed. *The Young Retarded Child: Medical Aspects of Care*, Baltimore, Maryland, Williams & Wilkins, 1973, Chapter 8, p. 81-97.

Malformation syndromes associated with MR are useful in diagnosis. Advances in such diagnosis have been chiefly due to the work of cytogeneticists and biochemists in their study of the cell and enzymes. The standard approach to the patient is a thorough history, examination, and investigation leading to diagnosis. The history may include family history as well as the details of pregnancy and the postnatal period. The examination confirms the etiological diagnosis and is the groundwork for assessing the child's disability. The examination may include methods and techniques which may specifically confirm the preliminary diagnosis, such as electrophoresis, urine screening, EEG, X-ray, nuclear sexing, and chromosomal analysis. The literature concerning MR and malformation syndromes is also helpful in final diagnosis of difficult cases. Syndrome identification and consultation is a growing service which will be helpful for future diagnosis. - *C. Wares.*

United Birmingham Hospitals
Birmingham, England

1720 **MOORE, J. R.** Comprehensive assessment. In: Griffiths, Margaret I., ed. *The Young Retarded Child: Medical Aspects of Care*. Baltimore, Maryland, Williams & Wilkins, 1973, Chapter 4, p. 29-40.

Comprehensive assessment may be utilized to discover the medical, social, and educational needs of handicapped children and to bring appropriate facilities to their aid. The assistance approach to handicapped children must be individual and must involve the family of such children. Early assessment and assistance are of the utmost importance from the medical, educational, and sociological viewpoints. The wide range of probable involvement of medical, educational, and sociological personnel and facilities necessitates a coordinated approach. The nature of assessment is longitudinal rather than singularly incidental. Medical personnel will be concerned with the history of the pregnancy and perinatal period and with the child's examination. Social workers will be primarily concerned with assessing the family and home environment. The nursery assessment is also a relaxed ground for examination for many members of the assessment team. Psychological and educational assessment may vary from intelligence testing to educational achievement. Language assessment may be performed by a speech therapist when appropriately indicated. Hearing assessment will be performed whenever development is obviously deficient at certain mental ages. Tests of visual acuity may be limited except in obviously deficient cases. Motor assessment may be performed by a physiotherapist both in handling and observation. Assessment reports are then assembled for review. Assessment centers might usefully be established. - *C. Wares.*

Birmingham Regional Hospital Board
Birmingham, England

1721 **RAINE, D. N.** Early detection by biochemical screening. In: Griffiths, Margaret I., ed. *The Young Retarded Child: Medical Aspects of Care*. Baltimore, Maryland, Williams & Wilkins, 1973, Chapter 3, p. 20-28.

Beginning in 1953, methods for detecting inherited metabolic diseases have been developed. Phenylketonuria may be detected by use of the ferric chloride nappy test (Phenistix), the L.I. Woolf chromatography test, the Robert Guthrie blood test, and McCamen and Robins' blood test. Other amino acid disorders may be discovered using the Guthrie test with modifications. Galactosemia may be detected by paper chromatography or by an enzymatic method. Lead intoxication is detected by atomic absorption spectrophotometry. Screening programs should be evaluated in terms of defining the problem or disease being looked for, the position before screening (incidence, natural history, prevention), the position anticipated after screening (effectiveness of methods of detection and treatment), answerability of required questions, how further information may be obtained, and how the program should be initiated. The future of screening depends upon the development of new systems for screening and screening management. - *C. Wares.*

United Birmingham Hospitals
Birmingham, England

1722 **GRIFFITHS, MARGARET I.** Early detection by developmental screening. In: Griffiths, Margaret I., ed. *The Young Retarded Child: Medical Aspects of Care*. Baltimore, Maryland, Williams & Wilkins, 1973, Chapter 2, p. 11-19.

Early identification of children with potentially handicapping conditions may be accomplished by screening in infancy. Screening for signs of abnormal development must necessarily depend on an understanding of the underlying processes and results of normal maturation. General screening techniques include the Gesell and Armatruda test, Griffiths developmental scale, Sheridan's scale, the Denver Developmental Screening Test tests, by Egan, Illingsworth, and Sheridan, Caldwell and Drachman scales, Frances-Williams and Yule comparison scales, Wood's scale, Tanner *et al.* height and weight charts, and Nellhaus skull circumference charts. Specific screening techniques include auditory screening, and screening of social behavior. Investigation in greater detail of children found retarded is necessary to specifically evaluate their problems and needs. - *C. Wares.*

1723 **GRIFFITHS, MARGARET I.** The young retarded child: introduction. In: Griffiths, Margaret I., ed. *The Young Retarded Child: Medical Aspects of Care*. Baltimore, Maryland, Williams & Wilkins, 1973, Chapter 1, p. 1-10.

Measurement of mental development is a complex and difficult task, dependent on variable diagnosis and subjective judgment. Both family and physician(s) must decide whether an individual child has a disability, the probable nature and cause, the degree of handicap, and appropriate management of both child and family to prevent further handicap. The disability determined may involve a motor disorder, disorder of special senses, general ill health, speech and language disorders, MR, and emotional/social factors. Most retardation noticeable in the first two years of life has an organic cause, such as genetic abnormality, acquired MR due to prenatal factors, perinatal insults, or postnatal effects. The incidence of development retardation (7% of young children) suggests that services for such children and their families are important. These services can enable the majority of such children to grow up able to live and function in the general community. Increased knowledge of conditions causing MR would greatly aid in its prevention. - *C. Wares.*

Institute of Child Health
University of Birmingham
England

1724 **MUNSICK, ROBERT A.** Hazards of amniocentesis. *Obstetrics and Gynecology*, 41(4):628, 1973. (Letter)

Reference is made to an article by Ryan et al. regarding the dangers of fetal bleeding in carrying out amniocentesis and an additional measure of management is suggested. Because of the high fetal risk of exsanguination, additional steps are suggested upon finding that the amniocentesis-obtained blood is fetal in origin. The first of these is amnioscopy when possible, at 30 min and at hourly intervals for several hours to discern a visual change in color due to bleeding; and the second step is a Kleihauer-Betke staining of a maternal blood film for quantitative readings of feto-maternal hemorrhage carried out immediately and at hourly intervals. - *A.C. Schenker.*

University of New Mexico
School of Medicine
Albuquerque, New Mexico 87106

1725 **RYAN, GARY T.; & PEARSON, JACK W.** Hazards of amniocentesis. *Obstetrics and Gynecology*, 41(4): 628-629, 1973. (Letter)

In response to Dr. Munsick's suggestion for further steps in the management of possible fetal bleeding in the course of amniocentesis, the problem arising after obtaining the quantity of fetal blood lost is to know when immediate interference is required. In order to interpret the significance of the two steps suggested, the amniotic fluid volume as well as the fetal weight and/or blood volume would have to be estimated as well in order to establish the fetal blood loss. - *A. C. Schenker.*

William Beaumont General Hospital
El Paso, Texas 79920

1726 **JONASSON, LARS ERIK.** The clinical value of amniotic fluid analysis in pregnancies complicated by Rh-isommunization or hepatosis. *Acta Obstetrica et Gynecologica Scandinavica*, 52(2):113-130, 1973.

A total of 605 amniotic fluid samples were obtained by abdominal amniocentesis from 363 women in the last trimester of pregnancy, 81 cases representing normal pregnancies, 239 with isoimmunization and affected fetuses, 29 with hepatosis gravidarum, and 14 nonimmunized patients with other complications of pregnancy. The optical density at 450nm (ΔE_{450}), total protein, and progesterone content of the fluid were determined in all cases, and alkaline and acid phosphatases were determined on 172 consecutive samples from 110 pregnancies. Values were multiplied by 1,000, yielding the Color Index (CI). A fairly good correlation existed between CI values and cord blood hemoglobin levels for pregnancies complicated by severe hemolytic disease but not for those with less severe disease. CI values and trends appearing before week 37 had greater predictive value than later observations. Contrary to expectations, a poor correlation was found between CI values and cord serum bilirubin concentrations in severe hemolytic disease. Cases with hepatosis showed a clear correlation between CI values and maternal serum bilirubin levels. CI values correlated with amniotic fluid total protein content both in normal pregnancies and in Rh-isoimmunized patients with affected fetuses. Determination of acid and alkaline phosphatase activity did not seem to provide any clinically important information with respect to Rh-isoimmunized patients. (46 refs.) - *B. J. Grylack.*

University Hospital
S 750 14 Uppsala, Sweden

1727 **GUIBAUD, S.; BONNET, M ; THOULON, J. M.; & DUMONT, M.** Alpha$_1$-antitrypsin in amniotic fluid. *Lancet*, 2(7825):379, 1973. (Letter)

Investigation of alpha$_1$-antitrypsin (A_1-AT) levels in 227 amniotic fluids obtained at various stages of gestation by simple radial immunodiffusion testing showed a progressive decrease in A_1-AT concentration in amniotic fluid with advancing pregnancy. Mean levels of total protein declined similarly, the 2 constituents having a significant correlation ($r=0.55$, $p<0.001$). No A_1-AT deficiency in amniotic fluid was found in 5 newborn infants with hyaline membrane disease, indicating the unreliability of this measure in some pathologic pregnancies. - *B. J. Grylack.*

Hopital de la Croix-Rousse
69004 Lyon, France

1728 **TOMLINSON, A. H.; & MACCALLUM, F. O.** Virus antigen in cells of lumbar cerebrospinal fluid. *Lancet*, 1(7798):319-320, 1973. (Letter)

The early diagnosis of herpes-simplex encephalitis by the use of the immunofluorescence technique on cerebrospinal fluid (CSF) cells is questioned, inasmuch as attempts to use such technique in known cases were unsuccessful. Certain aspects of the report by Dayan and Stokes are found unconvincing, particularly in reference to the quality of the reagents used, which were not adequately documented. There is no mention of the species specificity of the conjugated antiglobulins used to detect virus antigen; it would also be of interest to know the numbers, as opposed to percentage, of fluorescent cells. An important piece of information, which was omitted, is whether virus was cultured from any or all of the fluids containing antigen-bearing cells. The immunological procedure is valueless unless the controls of specificity are beyond doubt. - *A. C. Schenker.*

Radcliffe Infirmary
Oxford OX2 6AH, England

1729 **ZUCKERMAN, JAMES E.** Human placental lactogen and the management of high-risk pregnancy. *Lancet*, 1(7796):200, 1973. (Letter)

The prognostic significance of the measurement of human placental lactogen (HPL) is discussed in reference to proposals suggesting this test as a routine screening procedure in pregnancy. To ascertain the normal range of (HPL) throughout the last half of pregnancy, and to evaluate the optimum period in gestation to begin prospective serial analysis of HPL, 173 normal pregnancies were studied in the antenatal clinics of Boston Hospital for Women. When the results of serum HPL were analyzed, the slope was found to be significantly steeper during weeks 31-40. The indication is that meaningful information can be derived from the serial measurements of HPL begun after the 30th week, as a means of predicting the outcome of pregnancies at high risk for fetal jeopardy. (8 refs.) - *A. C. Schenker.*

Harvard Medical School
Boston, Massachusetts 02115

1730 Detecting the fetal heart. *British Medical Journal*, 3(5838):445, 1972. (Editorial)

A new ultrasound technique permits the rapid detection of fetal heart beats as early as 7 wks gestational age. This technique will permit detection of fetal death, hydatiform mole, blighted ovum, and pelvic tumors, so that proper treatment can be initiated earlier. There is no evidence that ultrasound is teratogenic. (7 refs.) - *V. J. Goldberg.*

1731 **GAIRDNER, DOUGLAS.** Ultrasonic fetal cephalometry. *British Medical Journal*, 3(5826):585, 1972. (Letter)

The development of the technique of ultrasonic fetal cephalometry will make it possible to follow continuously the growth of an individual through both prenatal and postnatal phases. Data from the curve for biparietal diameter by ultrasound obtained by Campbell and Newman (1971) were taken and multipled by an arbitrary factor 3.5, to allow for the elliptical shape of the head, in order to determine how estimates of fetal head size as obtained by ultrasonic cephalometry agreed with those obtained by measurement of head circumference after birth. Satisfactory agreement of biparietal diameter X 3.5 with observed head circumference was obtained. (3 refs.) - *B. J. Grylack.*

Addenbrooke's Hospital
Cambridge, England

1732 **DAVIES, P.** Ultrasonic fetal cephalometry. *British Medical Journal*, 3(5826):585, 1972. (Letter)

Different types of ultrasonic apparatus appear to give different values for the fetal biparietal diameter. Therefore, information must be obtained concerning the apparatus and technical criteria used by Dr. P. Flamme in the largest series of biparietal diameter measurements published so far, before his results can be applied by other researchers. (5 refs.) - *B. J. Grylack.*

City Hospital
Nottingham, England

1733 **VASS, L.; & SELLYEI, M.** Modified technique for banding human chromosomes. *Lancet*, 2(7786):1093, 1972. (Letter)

Empirical modification of the 2 X SSC method for banding human chromosomes by staining with preheated Giemsa solution for 2 minutes at 40-45° C, instead of staining at room temperature, consistently produced banding in at least 70% of mitoses; 4 X SSC incubation in Giemsa solution at 40-45° C produced similar results for flame-dried specimens: and about 50% of mitoses were banded by staining with Merck's Giemsa powder at room temperature, although staining with this solution was not successful at 40-45°C. Chromosome bands appear to be stained at different temperatures because of the varying qualities of the Giemsa solutions. (5 refs.) - *B. J. Grylack.*

Robert Karoly Hospital
Budapest XIII, Hungary

1734 **ROBINSON, HUGH P.:** Detection of fetal heart movement in first trimester of pregnancy using pulsed ultrasound. *British Medical Journal*, 3(5838):466-468, 1972.

A sonograph which can display simultaneously 2 of 3 modes can be used to detect fetal heart movements across the abdominal wall. Of 56 patients who were less than 15 wks pregnant

(menstrual age), fetal echoes and heart beats and continuing pregnancy were found in 42. Fourteen of 56 subsequently aborted; of these, fetal heart beats had been detected in 3. The fetus was identified but no heart movements were found in 4, blighted ovum was found in 6, and missed abortion in 1. Fetal heart movements can be detected as early as the 48th day of amenorrhea, and this technique can be used to monitor patients with threatened or recurrent abortion and to manage many problems of early pregnancy. (15 refs.) - *V. J. Goldberg.*

University of Glascow
Glascow, Scotland

1735 **STICKLER, GUNNAR B.** Take it easy when evaluating the mentally retarded child. *Clinical Pediatrics*, 11(7):373, 1972.

Current practices in evaluating the MR child are all too often needlessly wasteful of manpower and money. The actually necessary testing procedures, laboratory tests, and consultations with specialists will routinely vary from one child to the next. Pediatricians should use their training and experience wisely to help eliminate the overly elaborate evaluation procedures so characteristic of current medical practice in the MR field. - *N. Mize.*

Mayo Clinic and Mayo Foundation
Rochester, Minnesota 55901

MEDICAL ASPECTS—Prevention and Etiology (General)

1736 **LEONARD, CLAIRE O.; CHASE, GARY A.; & CHILDS, BARTON.** Genetic counseling: a consumer's view. *New England Journal of Medicine*, 287(9):433-439, 1972.

A survey of parents of children with cystic fibrosis, phenylketonuria, and Down's syndrome who had received genetic counseling was designed to discern the parents' understanding of such counseling. The questionnaire revealed that only half had a good understanding of the information given, ¼ had some understanding, and ¼ gained very little. The burden felt in bearing and caring for a defective child appeared to be a stronger determinant of attitudes toward reproduction than a knowledge of precise risk figures. Barriers to use of information included religion, emotional conflict, lack of grasp of probability, and lack of knowledge of genetics and human biology. Genetic counseling is a branch of preventive medicine and as such its techniques and results should be evaluated thoroughly. (12 refs.) - *N. Jarvis.*

Johns Hopkins Hospital (Pediatrics)
Baltimore, Maryland 21205

1737 **GAYLIN, WILLARD.** Genetic screening: the ethics of knowing. *New England Journal of Medicine*, 286(25):1361-1362, 1972. (Editorial)

The report of a safe and accurate test for presymptomatic detection of Huntington's chorea may prompt debate of the ethical validity of screening techniques for incurable disease. In the spirit of a free society diagnostic research should be continued with consideration to abridgement only in dire social circumstances. Perfected diagnostic procedures and their availability should be publicized and not be inhibited by fears of patient acceptance. Legally mandated testing should be avoided since Huntington's chorea presents no threat to the general population and its implementation would abrogate a patient's right to know, early or late, of his fate. Ultimately the decision to utilize the procedure should continue to come from the consideration of the patient's and doctor's needs to know. (2 refs.) - *V. J. Goldberg.*

New England Journal of Medicine
Boston, Massachusetts 02115

1738 Research Group on Ethical, Social and Legal Issues in Genetic Counseling and Genetic Engineering of the Institute of Society, Ethics and the Life Sciences. Special Article: Ethical and social issues in screening for genetic disease. *New England Journal of Medicine*, 286(21):1129-1132, 1972.

Since genetic screening programs such as those for sickle-cell anemia and Tay-Sachs disease are becoming widespread and in some cases compulsory, ethical, social, and legal questions raised by these programs must be answered. Such programs must define their goals, among which improving the health of persons with genetic diseases, pro-

viding information for informed choices in reproduction, and alleviating familial and social anxiety about genetic disease are the most acceptable. Acquisition of knowledge about genetic diseases should be secondary to these goals; reduction of deleterious gene frequency cannot be considered primary because of serious moral and ethical problems involved. Screening programs should have an attainable purpose, involve the community in administration and review, be accessible to all, utilize adequate testing procedures, and be conducted on a voluntary basis with informed consent of participants under guidelines governing human experimentation. They should practice full disclosure of all unambiguous results to the participant or his agent, include nondirective genetic counseling, provide information on the nature and cost of available therapies, and ensure the rights of privacy of participants. Every effort should be made to avoid stigmatization through widespread undesirable labeling of individuals on a genetic basis. (16 refs.) - *N. Jarvis.*

Institute of Society, Ethics and the Life Sciences
Hastings-on-Hudson, New York 10706

1739 **VALENTINE, G.H.** Reproductive counselling services. *Canadian Medical Association Journal*, 106:757-759, 1972.

The well-justified public demand for information on the outcome to be expected from reproductive activity can be met best by a reproductive counselling clinic located in a major medical center, staffed at least by a clinical general pediatrician, clinical geneticist, gynecologist-obstetrician, psychiatrist, and social worker, and providing access to a small number of beds in a pediatric as well as a gynecologic facility. The clinic should be research oriented. - *B. J. Grylack.*

War Memorial Children's Hospital
London 15, Ontario, Canada

1740 Measuring placental function. *British Medical Journal*, (5794):193-194, 1972.

Various biophysical and biochemical techniques for measuring fetoplacental function have been developed as a consequence of the greater concern for the welfare of the fetus *in utero*. Continuous fetal heart monitoring and scalp sampling are used to observe the fetal state during labor. Simple amnioscopy has proved less valuable than staining and examining desquamated fetal cells in amniotic fluid with Nile blue sulfate. Ultrasonic scanning may be useful in assessing fetal growth. Serial estimations of urinary estriols on 24-hour specimens are thought generally to provide the most valuable index of fetoplacental function, but measurement of plasma estriol and plasma progesterone with new protein-binding techniques may prove to reflect fetal status more accurately. In recent years the search for a good test of placental function has turned to some other enzymes and hormones, cystine-aminopeptidase, heat-stable alkaline phosphatase, and human chorionic somatomammotrophin among them, which remain to be evaluated fully as predictors of fetal function. (12 refs.) - *B. J. Grylack.*

1741 **EDWARDS, J. H.** Genetic counselling. *British Medical Journal*, 2(5807):229, 1972. (Letter)

Genetic counseling is an emotional field in which hopes often dominate facts. To state that parents make sensible use of information they are given on the chances of a particular genetic disorder in a family recurring in future generations means that they are the recipients of the advice the donor wishes to give. Similarly, any hope for gradual reduction of the number of children born with genetically determined disorders implies an extension of genetic counseling to include selective abortion. If, in fact, the various specialists are not competent to advise on genetic questions, perhaps attention should be paid to improving their education and their facilities or to establishing a supplementary service. - *B. J. Grylack.*

Infant Development Unit
Birmingham Maternity Hospital
Birmingham, England

1742 Intelligence and fertility. *British Medical Journal*, 2(5806):125-126, 1972.

Acceptance of the possibility of transition from a population in balance as a result of high fertility and high childhood mortality to one in balance as a result of planned small families and decreased childhood mortality has brought with it fear of a lowered average genetic fitness of the general population. The expectation that differential fertility would be a transient phenomenon and would tend to disappear with the spread of effective family planning throughout the community has been justified in the United States as

well as in Europe and the United Kingdom. A positive correlation of fertility and IQ is perhaps to be expected once all children are planned. While there is a need for Britain and the rest of Europe to achieve a mean family size at the replacement rate of 2:1 in the near future, variation in the size of families is important and must continue. (7 refs.) - *B. J. Grylack.*

1743 **SAMPSON, PAUL.** Just what makes embryologic development go wrong? A warning about introducing new teratogens. *Journal of the American Medical Association*, 221(8):853, 1972.

During a recent meeting of the American Association of Pathologists and Bacteriologists in Cincinnati, Ohio, Dr. Samuel S. Epstein, M.D., Professor of Pharmacology at Case Western Reserve University School of Medicine, strongly advocated the most stringent possible restrictions on suspected teratogens and proposed a national registry of birth defects in order to trace the epidemiology of congenital anomalies and thus to identify and aid individuals at risk. Although it was claimed in an article on the prenatal effects of the herbicide 2,4-D on rats that this herbicide was not a teratogen, signs of embryotoxicity and fetotoxicity were seen in the fetuses of pregnant rats exposed to it. In view of the significantly greater sensitivity of humans to the teratogenic effects of thalidomide as compared with animals and the fact that standard test systems are extremely insensitive, the only reasonable policy is to take as few risks as possible. - *B. J. Grylack.*

1744 **SAMPSON, PAUL.** Just what makes embryologic development go wrong? Congenital disorders spur growing interest. *Journal of the American Medical Association*, 221(8):848-849, 1972.

Some generally accepted principles of teratology were reviewed at the recent meeting of the American Association of Pathologists and Bacteriologists in Cincinnati, Ohio. Susceptibility to teratogenesis varies with the genotype of the conceptus, the manner in which interaction with the environment occurs, and the state of development of the embryo. Different teratogens act variously, the nature of the particular agent influencing its access to the conceptus. Deviant manifestations, which become more frequent with increasing dosage, can take the form of death, malformation, growth retardation, and functional disorder. - *B. J. Grylack.*

1745 **SAMPSON, PAUL.** Just what makes embryologic development go wrong? Molecular events leading to defects remain unclear. *Journal of the American Medical Association*, 221(8):849, 853-854, 1972.

Debate occurring at the recent meeting of the American Association of Pathologists and Bacteriologists in Cincinnati, Ohio, emphasized that differences in definitions, albeit minute, could have important influences on the understanding of the mechanism underlying teratogens and, ultimately, on the prevention of avoidable birth defects. The process by which the homogenous DNA in all somatic nuclei in an early embryo gives rise to differentiated cells appears to be one of induction, but uncertainty about the site of induction and the early molecular events in the process promotes speculation on the existence of a whole variety of target sites. In the meantime, fragments of empiric evidence have led to sharp differences in opinion concerning whether or not an undifferentiated cell exists and concerning distinctions between proliferative and quantal cell division cycles. - *B. J. Grylack.*

1746 **EPSTEIN, CHARLES J.; & GOLBUS, MITCHELL S.** Role of prenatal genetic studies. *New England Journal of Medicine*, 288(26):1413, 1973. (Letter)

Reference is made to Garlinger's letter objecting to the restrictive policy regarding amniocentesis. A policy of discouraging this procedure if a decision against abortion has already been made is not equivalent to one requiring abortion if the fetus is abnormal. The ultimate decision for or against abortion is made by the parents. The policy of discouraging amniocentesis in circumstances in which abortion is definitely rejected as a possible alternative is based on the fact that the data necessary to validate its safety and to define the risks precisely do not exist. The suggestion that failure to follow a policy of unrestrictive consent leads to discrimination along socioeconomic lines is wholly unfounded in the program under discussion. - *A. C. Schenker.*

University of California
San Francisco, California

1747 **MILUNSKY, AUBREY.** Role of prenatal genetic studies. *New England Journal of Medicine*, 288(26):1412, 1973. (Letter)

Objection to the restrictive policy of not providing amniocentesis and prenatal genetic studies unless the pregnant patient intends to have an abortion in the event of the finding of a defective fetus, voiced by Garlinger et al., is supported by an additional reason for an objection. Such restrictive policy distorts the aims of pregenetic studies. The emphasis of such studies is on providing life to the unaffected offspring, rather than on the removal of defective fetuses. The physician's responsibility should extend to referring patients elsewhere when the dictates of their own beliefs prevent them from doing amniocenteses. - *A. C. Schenker.*

Massachusetts General Hospital
Boston, Massachusetts

1748 **HUG, GEORGE.** Role of prenatal genetic studies. *New England Journal of Medicine*, 288(26):1412-1413, 1973. (Letter)

Objection to restrictive consent in the performance of amniocentesis, as stated in a letter to the editor, is supported by a case in point. The mother of a baby with Pompe's disease was again pregnant and insisted that the prenatal diagnosis be attempted although she did not want an abortion under any condition. She simply explained that she needed to know what to expect. Strict policies in these situations may reflect a lack of experience in prenatal diagnosis with those aspects of the procedure which involve the intellectual and emotional needs of the parents, their families, and the public at large. - *A. C. Schenker.*

University of Cinncinnati College
of Medicine
Cincinnati, Ohio

1749 **CHAN, WAN H.; PAUL, RICHARD H.; & TOEWS, JUDY.** Intrapartum fetal monitoring: maternal and fetal morbidity and perinatal mortality. *Obstetrics and Gynecology*, 41(1):7-13, 1973.

Maternal and fetal morbidity associated with fetal monitoring over a 3-year period is reviewed. Maternal febrile morbidity was defined as an oral temperature of 100.4 F on any 2 of the first 10 days postpartum, exclusive of the first 24 hours. Of the 1,102 patients in whom an intrauterine catheter was used to assess labor, 3 uterine perforations occurred. In each instance, initial perforation was likely caused by the relatively rigid catheter guide rather than by the catheter itself. Maternal febrile morbidity was higher in clinic as compared to private patients: 3.5% in private and 9.7% in monitored clinic patients. In both these groups morbidity was more often associated with cesarean section or urinary tract infections and was probably unrelated to fetal monitoring. Endometritis was noted in only 6 of the total monitored group of 1,150 patients. There were no scalp abscesses among the 1,121 monitored labors in which fetal scalp electrodes had been applied. Two intrapartum stillbirths occurred among patients in the monitored group, both from intrauterine asphyxia. It is possible that the 2 fetuses could have been salvaged, but it is also possible that deaths in the nonmonitored group could have been prevented by fetal monitoring of high-risk patients. (6 refs.) - *A. C. Schenker.*

Los Angeles County-Martin Luther
King, Jr., General Hospital
Los Angeles, California 90059

1750 **DIDDLE, A. W.** Rights affecting human reproduction. *Obstetrics and Gynecology*, 41(5):789-794, 1973.

The controversy regarding elective abortion is discussed in terms of individual rights, legislative ruling, and medical ethics. Arguments advanced against permissive legislation in this matter include the rights of the unborn child, and the religious or moral view that abortion is demeaning to human life. On the opposite side of the controversy it is argued that if we are to avoid a population explosion, the family should be entitled to have children without defects, an argument in favor of genetic counseling; that the role of the law in protecting the unborn child's life is beyond its designated powers, as is its jurisdication with respect to sterilization. The unwanted child poses a problem to physicians in terms of medical ethics; the rights of the mother as well as that of the child are involved. (32 refs.) - *A. C. Schenker.*

Memorial Research Center and Hospital
University of Tennessee
Knoxville, Tennessee

1751 **BRENNAN, MARY E.** Prevention: medico-social aspects. In: Griffiths, Margaret I., ed. *The Young Retarded Child:*

Medical Aspects of Care. Baltimore, Maryland, Williams & Wilkins, 1973, Chapter 18, p. 184-198.

MR may be caused by genetic abnormality or by environmental hazards before or after birth. Social factors related to brain damage include the distribution of material resources (affecting nutrition and infection), environmental hazards and pollution (poisoning, radiation, accidents and trauma, and battering), and family building patterns (maternal age, parity, and prematurity). Social factors related to the development of psychological constructs may include environmental stimulation, development of attitudes antipathetic to learning, and the social deprivation syndrome. Social factors related to the development of functional disability include stigmatization and social attitudes. Medical policies for preventing MR depend primarily on the availability and acceptability of services, involving principles of health education, services before and during pregnancy, childhood attention and screening, and contraceptive guidance. Services for the disabled are also generally preventive. Social policies for preventing MR are related to tax policies, housing, health, education, and community participation in health services. An appropriate social structure in combination with adequate medical services can prevent a large proportion of MR. - *C. Wares*.

University of Birmingham
Birmingham, England

1752 **EDWARDS, J. H.** Prevention: genetic counselling. In: Griffiths, Margaret I., ed. *The Young Retarded Child: Medical Aspects of Care*. Baltimore, Maryland, Williams & Wilkins, 1973, Chapter 15, p. 164-171.

Genetic counseling is usually recommended in cases of MR or the likelihood of its occurring according to individual or family history. Counseling may involve guidance concerning contraception (sterilization, abortion, or selective abortion), recurrence risks (as chromosomal or genic disorders), and specialized information on disorders not due to simple chromosomal and genic defects. Fertility and conception control for the purposes of preventing incidence of MR remains a large problem for genetic counselors. - *C. Wares*.

University of Birmingham
Birmingham, England

1753 **WOOD, B.S.B.** Prevention: perinatal factors. In: Griffiths, Margaret I., ed. *The Young Retarded Child: Medical Aspects of Care*. Baltimore, Maryland, Williams & Wilkins, 1973, Chapter 16, p. 172-178.

Perinatal factors associated with mental handicap in surviving infants may include both environmental and medical entities. Environmental factors predictive of perinatal mortality or handicap include low social class, extremes of age, small stature, and high parity. Medical factors include pre-eclamptic toxemia, antepartum hemorrhage, anemia, and smoking. These factors may be the cause of premature infants or light-weight infants, which are statistically susceptible to MR or handicap. Cognizance of these factors can usefully affect medical care in the reproduction process, including pregnancy, labor, and neonatal period. Antenatal considerations include maternal diabetes, chronic hypertension, chronic renal disease, pre-eclamptic toxemia, prolonged rupture of membranes, bad obstetric history, and rhesus incompatibility. Labor considerations are primarily concerned with fetal distress. Neonatal problems may include resuscitation of the infant at birth, cerebralism, feeding, infection, hyperbilirubinemia, and other common problems. The physiological processes of reproduction should be knowledgeably managed with these factors in mind. - *C. Wares*.

United Birmingham Hospitals
Birmingham, England

1754 **ROSE, LESLIE I.; GABBE, STEVEN G.; TEICHHOLZ, LOUIS E.; VILLEE, DOROTHY B.; &*WILLIAMS, GORDON H.** Medical intelligence: Dermatoglyphics associated with fetal wastage. *New England Journal of Medicine*, 287(9):451-452, 1972.

Three of 25 patients with fetal wastage vs none of 58 normally fertile women demonstrated whorls on all 10 digits ($p > 0.01$). Two of 3 had given birth to at least one normal child. The presence of 10 whorls and a history of miscarriage may be associated with the possibility of future miscarriages so that pregnant women with this characteristic should be given intensive care. (10 refs.) - *V. J. Goldberg*.

Peter Brent Brigham Hospital
Boston, Mass 02115

1755 Facts about abortions. *British Medical Journal*, 2(5864):438, 1973. (Editorial)

Some statistical details regarding abortions are given with respect to the figures of 1971, in which over 100,000 terminations were carried out in England and Wales. Of 126,777 operations, nearly 95,000 were on residents of England and Wales and a further 2,000 on women from other parts of the British Isles. Of the foreign women, 12,000 were French and 13,500 German. Over half the terminations were in single women, the majority of whom had had no liveborn children, while almost all were aged 24 or less. All but 7,000 of the 42,000 married women had had 2 or more children, and most were aged 30 or above. Sterilization was carried out at the same time as abortion in 14,000 cases in the women at risk, including 343 single women. The 2 most common abortion techniques were dilation and curettage, used in 58,000 cases, and vacuum aspiration, used in 53,000, of which 45,000 were less than 13 weeks' gestation. Abdominal hysterectomy was used in 11,000 cases and hysterectomy in another 1,000, mostly women aged 30 or over. There were 11 deaths: in 6 the termination had required either hysterectomy or hysterotomy. In 7 of these cases the abortion procedure was thought to be directly responsible. (1 ref.) - *A C. Schenker.*

1756 **SMITHELLS, R. W.; & BEARD, R. W.** Research investigations and the fetus. *British Medical Journal*, 2(5864):464-468, 1973.

A discussion devoted to problems of research investigations and the fetus is submitted, followed by a discussion of the legal aspect. The argument from the viewpoint of the pediatrician (Dr. Smithells) is based on the premises that the young child (or a fetus) cannot give valid consent; the parent(s) should therefore be approached for informed consent and a third person be present to insure that this is freely given. It is essential that any ethical code relating to clinical research should err in the direction of stringency rather than laxity. Justification for fetal research from the obstetrician's viewpoint (Dr. Beard) is argued as a progressive concept in the prevention of congenital defects. It is important to distinguish between the viable and nonviable fetus. With the mother's consent, the investigator must take every precaution as to the safety of the procedure, and the protocol should be acceptable to an ethical committee and to the parents before any study is undertaken. From the legal viewpoint (by a barrister) treatment is paramount; no medical procedure involving the slightest risk or accompanied by the slightest pain may be inflicted on a child for research reasons alone. A discussion includes: the present legal position; are researchers indemnified; and what to tell the parents. (5 refs.) - *A. C. Schenker.*

1757 **DENNIS, K. J; DIGGORY, PETER; & MACGILLIVRAY, IAN.** Latent morbidity after abortion. *British Medical Journal*, 2(5866): 611, 1973. (Letter) ,

The report by the Wynns, which is commended in a leading article in this journal, has been contradicted as to interpretation by Dr. Potts and Dr. Ogborn in two separate articles. The interpretation of the risks of subsequent ectopic pregnancies, following abortion, low-birth-weight babies, and congenital malformations is considered erroneous. The Wynns have misquoted and misunderstood the findings of the 1958 British Perinatal Mortality Survey. The uncritical leading article gives this report the implied authority of the medical establishment and has thus been interpreted by the national press, much to the alarm of about half a million women who have obtained abortions in this country. - *A. C. Schenker.*

University of Southampton
Southampton, England

1758 Genetic disease. *Nature*, 238(5358): 7, 1972. (Editorial)

An increase in medical genetic services is recommended by a World Health Organization (WHO) scientific group in a recent report. The aim of the report is to furnish reliable information on the effects of treatment and prevention on genetic diseases. Interest in medical genetics has increased with decrease in morbidity and mortality due to infections, infestations, and malnutrition. Medical genetic services should be made available to all doctors, and counseling should be available at each medical school. A need for more research into prenatal diagnosis is stressed, and it is recommended that children born after amniocentesis be studied to assess the long-term effects of this procedure. - *A. C. Schenker.*

1759 **OBERMAN, J. WILLIAM.** The high risk infant: changing concepts. *Clinical Proceedings, Children's Hospital National*

Medical Center, 28(5):114-128, 1972.

With infant mortality showing only a slow decrease during the last decade, researchers have begun to alter various concepts and to seek new factors affecting neonatal status. The concept of prematurity itself has undergone a considerable change in recent years. There has been a resurgence of interest in oral feeding of infants of diabetic mothers before 24 hours of age in order to avoid high serum bilirubin concentrations, while enthusiasm for intrauterine transfusions in the management of erythroblastosis has moderated somewhat in favor of more conservative treatment. Neonatal screening programs for hyperphenylalaninemia are now operated in most states, and other metabolic diseases have been proposed as additions. Attempts to define further the basic processes leading to increased risk to mother and infant during pregnancy and childbirth have led to changing concepts in regard to intensive care units, transport systems for sick infants, newborn recovery rooms, hospitalization of mothers at risk, and comprehensive follow-up care for high-risk infants. (31 refs.) - *B. J. Grylack*.

Children's Hospital National
Medical Center
Washington, D. C.

1760 **LITTLEFIELD, JOHN W.** Genetic screening. *New England Journal of Medicine*, 286(21):1155-1156, 1972. (Editorial)

The comprehensive guidelines for genetic screening developed by the Institute of Society, Ethics and the Life Sciences, directed towards the numerous programs now starting to detect in high-risk ethnic groups those individuals whose genes threaten the health of their future offspring when combined with similar genes in their mates, are primarily cautionary and do not convey the enthusiasm held by some for genetic screening or its potential scope. Genetic screening has been concerned to date primarily with detection of the individual whose own health is threatened. The shift in attention to the detection of offspring-threatening genes represents a significant step. The intention of the new genetic screening raises new psychosocial and ethical problems, even if the screening is voluntary. Hopefully, people will assume a positive attitude towards the new screening, and some of the enormous biosocial problems confronting society will be managed more wisely. (7 refs.) - *B. J. Grylack*.

1761 **LOWE, C. R.** Congenital malformations and the problem of their control. *British Medical Journal*, 3(5825):515-520, 1972.

Definition and study of the environmental components of congenital malformations may show that some of them are amenable to control. Laboratory research on environmental influences has revealed some general principles, particularly relevant to the study of malformations in man, concerning the dose and teratogenic range of teratogens and the gestational periods at which different fetal organs are sensitive to teratogens. Indirect evidence of environmental influences relates to geographical differences, temporal differences, social class, maternal age and parity, and other factors. In a 3-year study of the prevalence of congenital malformations among women in a given area of South Wales, of the 102 infants born to 102 women with their first registered birth who reported 3 or more previous miscarriages, 12 had congenital defects. Direct evidence of the loss of high proportions of malformed fetuses by spontaneous abortion has been provided in a survey of the incidence of gross malformations in a very large population of early fetuses obtained from women whose pregnancies had been terminated artificially. Universal vaccination of girls against rubella and early diagnosis of syphilis are the only traditional preventive measures available. The need to control the hazard of pharmacologically induced malformations and to establish more effective methods of treatment still exists. (16 refs.) - *B. J. Grylack*.

Welsh National School of Medicine
Cardiff, Wales

1762 **HECHT, FREDERICK; & HOLMES, LEWIS B.** What we don't know about genetic counseling. *New England Journal of Medicine*, 287(9):464-465, 1972. (Editorial)

Genetic counseling techniques and results need to be investigated. More information is needed concerning the training of counselors, the medium of approach, the need for follow-up or repeated counseling, the assessment of information transmission, and the keeping of records. Other issues include whether greater efforts should be made to detect and counsel for common recessive diseases (sickle cell anemia and cystic fibrosis), common autosomal dominant but poorly understood diseases (Huntington's chorea), or common poly-

genic disorders (diabetes mellitus, essential hypertension, cleft palate/lip). The objectives, magnitude of demand, the feasibility of genetic registers, and the funding of counseling also need to be examined. (5 refs.) - *V. J. Goldberg.*

10 Shattuck Street
Boston, Mass

1763 **SPELLACY, W. N.; & BUHI, W. C.** Amniotic fluid lecithin/sphingomyelin ratio as an index of fetal maturity. *Obstetrics and Gynecology*, 39(6):852-860, 1972.

The amniotic fluid lecithin/sphingomyelin ratio (L/S) was determined using chromagen silica gel strips. In 190 amniotic fluid samples from 140 women, the mean curve exceeded a ratio of 2.0 after 35wks gestation. In 69 cases where L/S was measured within 1 wk of delivery, the ratio is correlated significantly with birthweight. There were significant correlations also between L/S and amniotic fluid bilirubin (Δ OD_{450}), Nile-blue staining fat cells, creatinine, and the ratio of amniotic fluid and maternal blood creatinine. Of 18 infants born within 1 week of the L/S measurement and having an L/S below 2.0, 6 developed RDS; the birthweights ranged from 550 to 3500g in this sample. In 17 infants with low birthweight (below 2500g) and low L/S measurement within 1 wk of birth, the L/S ratios were greater than 2.0; none developed RDS. This test is recommended for screening infants at risk for RDS when early delivery is being considered. (16 refs.) - *V. J. Goldberg.*

University of Miami School of Medicine
Miami, Florida 33152

1764 **MUNSICK, ROBERT A.** Air embolism and maternal death from therapeutic abortion. *Obstetrics and Gynecology*, 39(5):688-690, 1972.

A massive air embolism was induced during a therapeutic abortion when the cannula intended for vacuum suction of the uterine contents was mistakenly connected to the pressure outlet of a laboratory vacuum pump used in the procedure. Vital signs changed within 30 seconds of the uterine air insufflation, thoracotomy was performed, and cardiovascular function returned. The patient remained in decorticate rigidity until she died 10 wks later. The patient had been exposed to infectious hepatitis and had been given 10 to 12 rads during roentgenographic examinations, despite knowledge of the patient's amenorrheic state. It is recommended that greater precautions be used in diagnostic X-ray studies of women of child-bearing age, that uterine aspirators be used, and that the equipment be tested before each use. (3 refs.) - *V. J. Goldberg.*

University of New Mexico School
of Medicine
Albuquerque, New Mexico 87106

1765 **STEINBERG, CHARLES R.; BERKOWITZ, RICHARD L.; MERKATZ, IRWIN R.: & ROBERTS, RICHARD B.** Fever and bacteremia associated with hypertonic saline abortion. *Obstetrics and Gynecology*, 39(5):673-678, 1972.

In a retrospective study of complications during hypertonic saline abortion, it was found that 56 of 302 had fever, 6 had bacteremia, and 19 had surgical removal of placental fragments. The incidence of these complications among 43 patients in a prospective study was 11, 0, and 2, respectively. Onset of fever correlated with onset of labor (24 hrs after saline infusion). Of the total 67 cases of fever, 6 had bacteremia, 15 had infections without bacteremia, 1 had thrombophlebitis, 2 had allergic reactions, and 43 were unexplained. (12 refs.) - *V. J. Goldberg.*

Cornell University Medical College
New York, NY 10021

1766 Genetic counselling. *British Medical Journal*, 1(5798):458-459, 1972. (Editorial)

Counselling is complicated in conditions due to chromosomal anomalies, and the risk is high when the parent has a balanced chromosome anomaly. The estimate of risk is made from knowledge of the anomaly, the genotypes of the parents, and empirical experience. In cases such as congenital malformation of the heart or neural tube where there is no known gene or chromosome involvement, estimates of risk are made by studying families in populations similar to that of the patients. Mathematical models and computer programs can be used to make predictions and may be better than intelligent guesses. (4 refs.) - *V. J. Goldberg.*

1767 ABO blood groups and abortion. *British*

Medical Journal, 3(5836):314-315, 1972. (Editorial)

ABO incompatibility between mother and fetus may lead to ABO hemolytic disease and may be a cause of habitual abortion. In 78 abortuses, 35 were incompatible vs 17 predicted from the ABO frequency in the population. In cases of infertile mating where all known causes had been eliminated, 87.3% were ABO incompatible vs. 38.6% among fertile ratings. (14 refs.) - *V. J. Goldberg.*

1768 MUKHERJEE, ASIT B.; BLATTNER, PEGGY Y.; & NITOWSKY, HAROLD M. Quinacrine mustard fluorescence of sex chromatin in human amniotic fluid cell cultures. *Nature*, 235(5335):226-229, 1972.

Fluorescing sex chromatin and Y body in amniotic fluid fibroblast cultures is reported, in contradiction to previous reports on this subject. Fibroblast cultures from 11 pregnant women were derived from samples of amniotic fluid obtained by amniocentesis before therapeutic abortion from the sixteenth to twenty-fifth week of gestation. Slides were prepared by use of the fluorescent staining method using quinacrine mustard (QM). By this method, 7 of 11 specimens were identified as females and 4 as males by their characteristic fluorescent bodies. It is clear that the fluorescence of sex chromatin can be detected in certain cell types in certain conditions (such as cultured fibroblasts) but not in other circumstances. It is suggested that proteolysis may alter the composition of sex chromatin and that specific proteins as well as DNA may be involved in the binding of these fluorochromes. (8 refs.) - *A. C. Schenker.*

Albert Einstein College of Medicine
Bronx, New York 10461

1769 GARRISON, MORTIMER. The clinical and sociologic importance of stimulating infants and young children. *Clinical Pediatrics*, 11(10):553, 1972.

Recent findings which show that "total intervention" programs can reverse the usual decline in IQ characteristic of children growing up in urban slum areas raise anew a controversial ethical issue. If society is to take seriously its obligation to prevent MR, the recorded results of such maximum stimulation programs as the "Milwaukee Project" cannot be ignored. In Heber's experiments with a small group of ghetto children whose mothers had IQ's below 70, the children randomly assigned to experimental conditions had a mean IQ of 123 after 5 years of participation in the program. In contrast, the mean IQ of control children was 86. The implications of these findings challenge a whole society to consider urgently the overall human ecology question of the early childhood environment and its effect on the individual. - *N. Mize.*

Temple University
Philadelphia, Pa. 19122

MEDICAL ASPECTS—Infections, intoxications, and hemolytic disorders

1770 GIUSTINO, V.; DUDLEY, F. J.; & SHERLOCK, S. Thymus-dependent lymphocyte function in patients with hepatitis-associated antigen. *Lancet*, 2(7782):850-853, 1972.

Phytohemagglutinin (PHA) induced lymphocyte transformation was measured as an index of thymus-dependent (T) cell competence in 38 patients with hepatitis-associated antigen (HAA). PHA-induced lymphocyte transformation was significantly higher in patients with prolonged acute hepatitis who subsequently recovered and cleared the antigen than in controls or in patients with chronic aggressive or persistent hepatitis or carriers ($p<0.05$). This finding suggested the association of HAA persistence with impaired T-cell function. The results also showed that the presence of active liver cell damage is not responsible for the impaired lymphocyte response to PHA. It was indicated that therapy with corticosteroids during an attack of acute hepatitis could lead to the persistence of both HAA and the associated infective agent, which could result subsequently in either chronic hepatitis or the carrier state. (13 refs.) - *B. J. Grylack.*

Royal Free Hospital
London WC1X 8LF, England

1771 DIETZMAN, DALE; HORTA-BARBOSA, LUIZ; KREBS, HELEN M., MADDEN, DAVID L.; FUCCILLO, DAVID A.; & SEVER, JOHN L. Diagnosis of subacute

sclerosing panencephalitis by a simple spinal fluid gel precipitation test for measles. *Pediatrics*, 49(1):133-136, 1972.

The symptoms of subacute sclerosing panencephalitis (SSPE) are dementia, myoclonus, seizures, and coma which may become manifest 2-5 yrs. after clinical rubeola. The disease is attributed to chronic intracellular measles virus infection of the brain. Existing procedures for detection of SSPE call for facilities which are generally not available at most hospital laboratories. A double diffusion gel precipitation method of detection utilizing incubation (24 hrs.) of concentrated cerebral spinal fluid samples (10 fold concentration) and high titer SSPE rubeola antigen-gel solution was developed on the premise that the demonstration of hemaglutinin-inhibiting or complement-fixing antibodies in cerebral spinal fluid (CSF) is sufficient for SSPE diagnosis. Cerebral spinal fluid from 12 Ss affected with SSPE and 14 controls was tested in a blind study of the procedure's effectiveness. No false positive results were observed, as distinct lines of precipitation were evident in all the samples from SSPE patients. Sensitivity of the new detection method was judged to be comparable to rubeola complement-fixation and hemagglutination-inhibition analysis of unconcentrated CSF. (8 refs.) - *K. Der*.

National Insitute of Neurological
Diseases and Stroke
Bethesda, Maryland 20014

1772 **COONROD, J. DONALD; & RYTEL, MICHAEL W.** Specificity of counter-immunoelectrophoresis in bacterial meningitis. *Lancet*, 2(7781):829, 1972. (Letter)

There is evidence that a simple and rapid immunoprecipitin (counterimmunoelectrophoresis) method can help to establish an etiologic diagnosis in patients with meningitis due to pneumococci, meningococci, or hemophilus. It is also known that certain isolates of escherichiae and staphylococci contain antigens which can precipitate hemophilus type b antibody, but is is undetermined whether cerebrospinal fluid from patients with meningitis due to escherichiae or staphylococci will give precipitin bands with hemophilus antiserum in the counterimmunoelectrophoresis test. The specificity of this test can be maintained without a loss of sensitivity if the precipitin titer of the antiserum is selected carefully. (4 refs.) - *B. J. Grylack*.

Medical College of Wisconsin
Milwaukee, Wisconsin 53226

1773 **WARIN, J.F.; HARKER, P.; & MAYON-WHITE, R. T.** Measles in vaccinated children in Oxford 1971. *Lancet*, 2(7781):810-812, 1972.

A 1971 Oxford, England, measles epidemic involved 322 cases, 50 of them occurring in vaccinated children and thus yielding an attack rate of 5.8 per 1,000. The overall protection given by the vaccine was 83.7%. The attack rates were highest among vaccinated and unvaccinated children aged 5 to 7 years. These children tended to have been vaccinated the longest and to have received killed vaccine followed by live vaccine. The effect on vaccinated children was not found to be related to the number of susceptible children or to any fault in vaccination. (15 refs.) - *B. J. Grylack*.

Health Department
Oxford, England

1774 **WARD, R.; BORCHERT, P.; WRIGHT, A.; & KLINE, E.** Hepatitis B antigen in saliva and mouth washings. *Lancet*, 2(7780):726-727, 1972.

The detection of hepatitis B antigen (HB Ag) in saliva or mouth washings from 22 (51%) of 43 MR patients, all with high titers of HB Ag in serum, suggested the involvement of saliva in the transfer of hepatitis B infection. Occult blood was present in 53 of 66 samples of saliva, the samples containing blood being approximately equally divided between HB Ag positive and HB Ag negative salivas. A similar pattern was observed among the 13 samples of saliva negative for occult blood. The presence of occult blood in saliva, therefore, was not found to be essential to the presence of HB Ag in saliva. (6 refs.) - *B. J. Grylack*.

Children's Hospital of Los Angeles
Los Angeles, California

1775 **PEMBREY, MARCUS.** [Thyrotoxicosis in

twin.] *Journal of Medical Genetics*, 9(2):250, 1970. (Letter)

The fact that monozygotic twins may have shared a common circulation *in utero* could have considerable bearing on the case of a hypothyroid baby whose identical twin suffered from thyrotoxicosis at puberty. If it is presumed that the pattern of secretion of thyrotrophin releasing hormone by the hypothalamus is "set" at a particular response level sometime during fetal life, several hypotheses could explain the association of athyreotic hypothyroidism in twin A with hyperthyroidism in twin B. (2 refs.) - *B. J. Grylack*.

1776 **BRYCE-SMITH, D.** Lead-poisoning. *Lancet*, 2(7781):817-818, 1972. (Letter)

Despite reports that only blood lead levels above 80μg/100ml in adults constitute a potential health hazard and that it is extremely rare for any symptoms to occur below this level, there is good evidence in the medical literature that clinical symptoms of plumbism can appear in adults at levels well under 80μg/100ml. The concept of a toxic threshold value of 80μg/100ml for lead in the blood of adults should be abandoned as a hindrance to accurate diagnosis. (13 refs.) - *B. J. Grylack*.

The University
Whiteknights Park
Reading, England

1777 **HAMBLING, M. H.** Hand, foot, and mouth disease associated with Coxsackie A9 virus. *Lancet*, 2(7783):931, 1972. (Letter)

In what may have been the first published report of hand, foot, and mouth disease associated with Coxsackie A9 virus, information provided on neutralization of antibody titers was not accompanied by a description of the techniques used in estimating the neutralizing antibodies to either the prototype Coxsackie virus type A9 or the isolates. A valid comparison of titers cannot be made without this information. However, if the tests were performed under similar conditions, the variation between antibody titers to the prototype and the isolated agents is extreme. Further investigation is warranted, since it appears that the isolates, although established as Coxsackie type A9 viruses, have stimulated antibodies which neutralize the isolated virus but fail to neutralize the prototype strain. - *B. J. Grylack*.

Public Health Laboratory
Leeds LS15 7TR, England

1778 **CRICHTON, JOHN U.; DUNN, HENRY G.; MCBURNEY, ANNETTA KARAA; ROBERTSON, ANN-MARIE; & TREDGER, ENID.** Long-term effects of neonatal jaundice on brain function in children of low birth weight. *Pediatrics*, 49(5):656-670, 1972.

The subsequent course of thirty infants weighing 2,183g or less at birth with a maximum recorded serum bilirubin level of at least 20mg/100ml was compared prospectively with that of 60 controls matched for sex, birthweight, and gestational age at birth, 30 with a maximal neonatal serum bilirubin level of 11-19.9mg/100ml, and 30 with a maximum recorded level of less than 11mg/100ml. Mean IQ scores were only slightly and not significantly lower in the most severely jaundiced group after follow-up periods of from 4 to 11 years. This group had a significantly higher incidence of MR (IQ<70) than the other groups, most of the affected Ss being boys. Within this group the ultimate mean IQ of the 13 Ss without hemolytic disease who received an exchange transfusion was considerably higher, but not significantly so, than that of 14 similar infants who did not have a transfusion. The findings indicated that the effect of nonhemolytic jaundice per se on the ultimate intelligence and neurological status of low-birthweight infants without definite kernicterus is probably small, but large-scale studies of data from several centers are required to confirm this conclusion. (53 refs.) - *B. J. Grylack*.

University of British Columbia
Vancouver 9, British Columbia, Canada

1779 **GHOSH, A.; & HUDSON, F. P.** Oxytocic agents and neonatal hyperbilirubinaemia. *Lancet*, 2(7781):823, 1972. (Letter)

Of 197 consecutive neonates, excluding those under 2260g, those delivered by cesarean section, and those with blood group incompatibility, 24 (12.1%) had a maximum unconjugated-serum-bilirubin level of more than 12mg/100ml. Of the 197 deliveries, 97 did not receive an oxytocic agent, and only 6 infants (6%) of this group had hyperbilirubinemia of more than 12mg/100ml. Of

103 births occurring after an oxytocic drip, 18 (17.4%) had hyperbilirubinemia of over 12mg/100ml. The data suggest that this method of promoting labor may have a role in the production of neonatal hyperbilirubinemia. In the 14 cases of hyperbilirubinemia delivered after an oxytocic agent had been used, jaundice could not be attributed to hemolysis, prematurity, or hepatocellular damage. The mechanism of hepatic conjugation of serum-bilirubin could possibly be disturbed by administration of the oxytocic agent. (3 refs.) - *B. J. Grylack.*

Fazakerley Hospital
Liverpool 9, England

1780 TANNO, H.; FAY, O.; & RONCORONI, M. Virus-B hepatitis in saliva. *Lancet*, 2(7781):822-823, 1972. (Letter)

Observation of the transmission of virus-B hepatitis in 7 couples prompted a study of the saliva of 13 patients whose sera contained Australia (Au) antigen. Two patients had chronic hepatitis and had transmitted acute hepatitis to their spouses. Filtration of saliva and immunoelectrophoretic investigation revealed the immunoprecipitate in 5 of 6 patients with acute hepatitis, in 3 of 4 with chronic hepatitis, and in the 3 with postnecrotic cirrhosis. The 11 patients with Au antigen in saliva also had it in urine. (4 refs.) - *B. J. Grylack.*

Sanatorio Parque
Boulevard Orono 860
Rosario, Argentina

1781 FUJITA, KIMIO; & TAKAHASHI, MATSUO. Rapid and simultaneous detection of syphilis and Australia-antigen-positive blood. *Lancet*, 2(7782):880, 1972. (Letter)

Counterelectrophoresis was used to detect Australia antigen and syphilis in blood samples in a mountain village hospital in Japan. Although it provided results within an hour, the test's sensitivity was not entirely satisfactory. (1 ref.) - *B. J. Grylack.*

Saku Central Hospital
Minamisaku Usuda
Nagano, Japan

1782 PARTIN, JOHN C.; SCHUBERT, WILLIAM K.; & PARTIN, JACQUELINE S. Fatty acids and mitochondrial injury in Reye's syndrome. *New England Journal of Medicine*, 286(14):787-788, 1972. (Letter)

Tissue and plasma unesterified fatty acid metabolism merit careful study in Reye's syndrome. A transient reduction in albumin synthesis could accompany the great reduction in serum pre-beta-lipoprotein measured early in the course of the illness in 6 patients. If liver parenchymal albumin were reduced transiently at the time tissue free fatty acids were increased, toxic levels of the free fatty acids might be achieved in the liver. (2 refs.) - *B. J. Grylack.*

Children's Hospital Research Foundation
Cincinnati, Ohio

1783 BROWN, R. E.; & MADGE, G. E. Fatty acids and mitochondrial injury in Reye's syndrome. *New England Journal of Medicine*, 286(14):787, 1972. (Letter)

A chemically mediated and potentially reversible mitochondrial injury may be instrumental in the evolution of Reye's syndrome. Fatty acids, potential endogenous toxins capable of producing an encephalopathy and affecting both mitochondrial metabolism and structure, may be associated with Reye's syndrome. The use of insulin and glucose, agents that inhibit lipolysis and mobilization of fat, appears to prevent further episodes of the free fatty acidemia occurring in Reye's syndrome and thereby to allow the injured cells and their mitochondria to recover. (8 refs.) - *B. J. Grylack.*

Armed Forces Institute of Pathology
Washington, D. C.

1784 REINICKE, VAGN; DYBKJAER, ESBEN; POULSEN, HEMMING; BANKE, OLE; LYLLOFF, KIRSTEN; & NORDENFELT, ERIK. A study of Australia-antigen-positive blood donors and their recipients, with special reference to liver histology. *New England Journal of Medicine*, 286(16):867-870, 1972.

Of 24 blood donors with Australia (Au) antigenemia selected from 13,300 consecutive registered Danish voluntary blood donors, 10 gave blood to 22 recipients, with no subsequent evidence of acute hepatitis seen in any of them. A completely

normal liver biopsy specimen was found in 6 of the donors. Cirrhosis was discovered histologically only in 1 donor. No cases that could be classified histologically as acute hepatitis were discovered by liver biopsy among any of the Au-antigenemic donors. The apparent lack of infectivity among recipients might be correlated with the absence of acute and chronic hepatitis in the present series of donors. (11 refs.) - *B. J. Grylack.*

Department of Medicine B
Bispebjerg Hospital
Copenhagen, Denmark

1785 KRUGMAN, SAUL. Summary of the seminar. *American Journal of Diseases of Children*, 123(4):435-438, 1972.

A seminar was conducted on the clinical features, pathology, epidemiology, etiology, immunology, and prevention of viral hepatitis. Since the data presented showed that serum hepatitis, like infectious hepatitis, can be transmitted by contact as well as by parenteral inoculation, it was suggested that viral hepatitis, type A, be used to signify infectious hepatitis, and viral hepatitis, type B, to signify serum hepatitis in order to avoid confusion and be more precise. In view of the fact that the data confirmed the definite association of Australia antigen with viral hepatitis, type B, and the lack of its association with viral hepatitis, type A, the antigen generally referred to as Australia, hepatitis-associated, or serum hepatitis should be designated as hepatitis B antigen. The ultimate solution to the problem of viral hepatitis will depend significantly upon the isolation and cultivation of hepatitis viruses A and B. (19 refs.) - *B. J. Grylack.*

New York University Medical Center
New York, New York 10016

1786 LAVERDANT, CHARLES; & ANTOINE, HENRI. Immune serum globulin mass prophylaxis of hepatitis due to virus A in epidemic surroundings. *American Journal of Diseases of Children*, 123(4):434-435, 1972.

Administration of standard immune serum globulin followed by 2 epidemic spikes of hepatitis and subsequent appearance of icterus after a 3-month latency period in Ss who should have been protected emphasized the short-term, simple, passive immunity created by injection of immune serum globulin. After the 90-day period when antibodies persisted, the virus that had not been killed by the immune serum globulin provoked the appearance of hepatitis. In epidemic surroundings, immune serum globulin prophylaxis by a single injection proved to be a method with temporary efficacy only and was more harmful than useful. It delayed the appearance of the disease but seemed liable to expose clinically inapparent forms by grouping them in time. (2 refs.) - *B. J. Grylack.*

Ecole d'Application du Service
de Sante des Armees
75 Paris 5e, France

1787 GROSE, CHARLES; & FEORINO, PAUL M. Epstein-Barr and Guillain-Barre syndrome. *Lancet*, 2(7790):1285-1287, 1972.

Five patients aged 18 months to 27 years had the Guillain-Barre syndrome associated with Epstein-Barr virus, even in the absence of infectious mononucleosis. The sera from all 5 patients demonstrated higher titers against Epstein-Barr virus than any one of the control group sera. These titers (400-1,000) generally are presented only in sera from patients with acute infectious mononucleosis. The 2 patients who fulfilled the serologic criteria for mononucleosis confirmed the association of this disease with the Guillain-Barre syndrome. The other 3 patients, who did not manifest any serologic evidence of infectious mononucleosis during the observation period, may have had a short-lived rise in heterophile antibodies before neurologic symptoms developed. The uniformly high titers of Epstein-Barr virus antibody and the divergent heterophile and ox-cell-hemolysin results suggested that the Guillain-Barre syndrome in both younger children and adults may be a manifestation of Epstein-Barr virus independent of clinical infectious mononucleosis. (21 refs). - *B. J. Grylack.*

Albert Einstein College of
Medicine
Bronx, New York 1046B61

1788 PRIDMORE, B. R.; ROBERTSON, E. G.; & WALKER, W. Liquor bilirubin levels and false prediction of severity in rhesus haemolytic disease. *British Medical Journal*, 3:136-139, 1972.

Of 716 cases of rhesus hemolytic disease, analysis of liquor bilirubin yielded wrong predictions of severity in 80 cases, overpredictions being made in

56 cases and underpredictions in 24 cases. Nevertheless, 88.8% of cases were predicted correctly, and liquor bilirubin analysis remains probably the most accurate single method of predicting the severity of rhesus hemolytic disease. Ascertainment of placental location prior to amniocentesis, careful attention to clinical assessment of gestational age and assessment of cytologic and biochemical criteria in liquor associated with prediction of gestational age, and repetition of blood analysis in late pregnancy in cases where the fetus has been predicted to be at low risk will improve the accuracy of prediction. (11 refs.) - *B. J. Grylack.*

University of Newcastle
upon Tyne
England

1789 Arboviruses west and north. *Canadian Medical Association Journal*, 106:1149-1150, 1972. (Editorial)

Serologic evidence indicates that arboviruses are present in the western and northern regions of North America. Serologic identification of western equine encephalomyelitis virus has shown this virus to be the cause of some human infections west of the Rocky Mountains. Isolation of California encephalitis virus from mosquitoes collected in the Yukon Territory near Whitehorse had provided proof for the first time that an arbovirus is endemic in subarctic portions of Canada. Although no overt human infections with California encephalitis virus have been documented from the Yukon, serologic evidence of subclinical infection has been found at Dawson Creek, British Columbia and Rochester, Alberta, thus involving areas north of 60°N. Summer 1971 witnessed the northward spread of Venezuelan equine encephalitis from Central America into Texas and the association of arboviruses previously encountered on the prairies of western Canada with central nervous system infections of humans and horses in British Columbia. (14 refs). - *B. J. Grylack.*

1790 **DESJARDINS, PAUL D.; DODDS, J. R.; & WILLOUGHBY, H. W.** Rh-D isoimmunization in a triplet pregnancy. *Canadian Medical Association Journal*, 106:1000-1001, 1972.

An Rh-negative, sensitized 43-year-old woman whose husband was homozygous to D (probability 95%) gave birth to Rh-positive and affected triplets. The mother's anti-D titer did not change during pregnancy. The result of amniocentesis, a $\Delta O.D._{450}$ of 0.089 and creatinine value of 1.6 mg%, did not provide strong support for early termination of pregnancy, and the patient was allowed to go into labor spontaneously. Only the first infant required an exchange transfusion. The fetal outcome in this case justified the management. (4 refs.) - *B. J. Grylack.*

Royal Victoria Hospital
Montreal 112, P.Q., Canada

1791 **IWAKATA, S.; ELKERTON, L. E.; RHODES, A. J.; BULL, J. A.; & *LABZOFFSKY, N. A.** Antibody response in school children to live rubella vaccine (Cendehill strain) *Canadian Medical Association Journal*, 106:980-982, 1972.

The efficacy of the Cendevax live rubella virus vaccine was evaluated with 65 schoolchildren. Hemagglutination inhibition (HAI), complement fixation (CF), and immunofluorescence (IF) were employed for the establishment of antibody titers. Sixteen of the 65 children showed no demonstrable rubella HAI antibodies in their prevaccination serum samples. Of these vaccinees, 10 of 11 showed seroconversion with HAI titers ranging from 1:64 to 1:1024 (geometric mean 1:180), CF antibodies were demonstrable in 7 of 10, with the titers ranging from 1:4 to 1:16, and rubella-specific immunoglobulin (Ig) M antibodies were detected in 8 of 10 postvaccination serum sample. There was no increase in the HAI titer after vaccination in 49 vaccinees who had preexisting antibodies. No correlation was observed between CF and rubella-specific IgM antibodies. (16 refs.) - *B. J. Grylack.*

Ontario Department of Health
Toronto, Ontario, Canada

1792 **GLASS, LEONARD; RAJEGOWDA, B. K.; KAHN, ERIC J.; & FLOYD, MERCEDES V.** Effect of heroin withdrawal on respiratory rate and acid-base status in the newborn. *New England Journal of Medicine* 286(14):746-748, 1972.

Estimations of respiratory rates and acid-base status made on 22 consecutive neonates with manifestations of heroin withdrawal and on 19 infants of similar birthweight and gestational age

born to nonaddicted mothers confirmed the presence of a rapid respiration in infants with heroin-withdrawal symptoms. Among the symptomatic infants, Pco_2 levels were significantly elevated on the second, third, and fourth days of life. The normal or elevated blood pH present in these infants may afford protection against pulmonary hypoperfusion and possibly reduce the risk from bilirubin encephalopathy. Adverse effects of hyperventilation include increased evaporative losses through the respiratory tract and a decrease in ionized serum calcium as a result of respiratory alkalosis. A causative relation may exist between low ionized calcium levels and the myoclonic jerks occasionally seen in the respiratory distress syndrome. (14 refs.) - *B. J. Grylack.*

Harlem Hospital Center
New York, New York 10037

1793 **SOULIER, JEAN-PIERRE; BLATIX, CHARLES; COUROUCE, A. M.; BENAMON, D; AMOUCH, P.; & DROUET, J.** Prevention of virus B hepatitis (SH hepatitis). *American Journal of Diseases of Children*, 123(4):429-434,1972.

In addition to traditional preventive measures against virus B hepatitis (serum hepatits [SH], MS-2), new measures have been undertaken based upon the detection of Australia (Au) antigen and attempts at active and passive immunization against Au antigen. In a preliminary trial with 11 volunteers (CA 65 to 80 years), Au plus serum (titer 1/16 before heating and 1/4 after heating) did not immunize successfully. Of 7 volunteers receiving Au plus serum (titer 1/1024 before and after heating), 1 had a sharp increase in antibody level with no evidence of antigen, 1 had subclinical hepatitis with the lowest antibody, and 5 showed a rough inverse correlation between the Au antigen level (always low) and Au antibody. When specific anti-Au gamma globulins were administered to 24 adults and 3 children during the first week following transfusion or accidental contamination with Au-positive blood, Au antigen could not be detected in any of the 18 cases for whom biological data were available, and in no cases was the passively administered antibody detectable during the first 12 days. (13 refs.) - *B. J. Grylack.*

Centre National de Transfusion
6, rue Alexandre-Cabanel Sanguine
75 Paris 15e, France

1794 **SCHWARTZ, JAMES F.** Ataxia in bacterial meningitis. *Neurology*, 22(10):1071-1074, 1972.

Ataxia occurred in 6 young children with acute bacterial meningitis, 5 of whom had haemophilus influenzae meningitis. Ataxia was a prominent presenting feature of the illness in 4 patients prior to diagnosis. Only 1 of these 4 children had nuchal rigidity. Thus, ataxia of acute onset associated with fever, respiratory symptoms, vomiting, or lethargy in young children may be the presenting manifestation of meningitis, even in the absence of nuchal rigidity. The other 2 children had ataxia as a transient neurological manifestation during antibiotic therapy and recovery. In view of the concurrence of deafness due to cochlear involvement and ataxia as seen in one of the present cases, vestibular involvement may be responsible for ataxia in some instances. Cerebellar dysfuction may be a cause of ataxia without deafness, whether it occurs as an early manifestation or late sequel of bacterial meningitis. (19 refs.) - *B. J. Grylack.*

Emory University School of Medicine
Atlanta, Georgia 30303

1795 **KEENAN, WILLIAM J.; PERLSLIGHT, IRWIN J.; & SUTHERLAND, JAMES M.** Kernicterus in small sick premature infants receiving phototherapy. *Pediatrics*, 49(5):652-655, 1972.

Phototherapy failed to prevent kernicterus in 4 small sick immature infants, all of whom had complex clinical courses complicated by infection. The serum bilirubin levels of each of the infants decreased when they were treated with phototherapy, but the development of kernicterus was not prevented. It is possible but unconfirmed that photherapy adversely affected the bilirubin binding by serum albumin in these infants or that while lowering the serum indirect bilirubin levels it did not lower the total level of toxic pigment effectively. On the other hand, phototherapy may not have been initiated early enough. (11 refs.) - *B. J. Grylack.*

Children's Hospital Research Foundation
Cincinnati, Ohio 45229

1796 **VAS, STEPHEN I.; SPENCE, LESLIE; &**

GILMORE, N. J. Importance of family contacts of HAA-positive persons. *New England Journal of Medicine*, 286(14):788,1972. (Letter)

A 50-year-old woman with HAA-positive hepatitis had an 8-year-old son with Down's syndrome who had ended a 6-month stay in an inst for MR children 3 months before his mother's illness began. It was assumed, in the absence of proof, that the infection was introduced by the son, who acquired it in the inst and passed it on to all other family members except his father, who appeared to be free of infection. - *B. J. Grylack.*

McGill University
Montreal, Quebec, Canada

1797 **BAUMGARTNER, E. REGULA; & WICK, HUGO.** Normal propionate metabolism in 'non-ketotic hyperglycinemia.' *New England Journal of Medicine*, 286(14):784-785, 1972. (Letter)

Two newborn infants with life-threatening neurologic symptoms and definite hyperglycinemia did not manifest ketoacidosis, thrombocytopenia, or marked neutropenia. A diet free of the ketogenic amino acids failed to improve the severe symptoms in 1 patient, who became MR and died at 18 months of age. The other patient died at 3 weeks. Both had normal propionate metabolisms, and no methylmalonic acid was detected in the urine. The findings suggested that the disease in these 2 patients was distinct from ketotic hyperglycinemia and methylmalonic acidemia and should be termed 'nonketotic hyperglycinemia' until its primary enzyme defect is known. (5 refs.) - *B. J. Grylack.*

Universitats-Kinderklinik
Basel, Switzerland

1798 **JEQUIER, MICHEL; & DUFRESNE, JEAN-JACQUES.** Diagnosis of cryptococcal meningitis. *New England Journal of Medicine*, 286(14):785-786, 1972. (Letter)

The diagnosis of cryptococcal meningitis may be difficult but can be confirmed easily and quickly by cytologic examination of the cerebrospinal fluid by filtration on a Millipore filter. In 3 cases the diagnosis was made in this manner at the first cerebrospinal fluid examination. Mistaking *Cryptococcus neoformans* for a lymphocyte is not possible with this method, which is much more reliable than the india ink procedure on ordinary smears. (3 refs.) - *B. J. Grylack.*

Hopital Cantonal Universitaire
Lausanne, Switzerland

1799 **MIZUTANI, HIROMICHI.** Immunologic abnormalities in subacute sclerosing panencephalitis. *New England Journal of Medicine*, 286(14):786, 1972. (Letter)

Skin tests performed with measles antigen on children who had recovered normally from measles and were presently exhibiting a hemagglutination inhibition antibody titer above 1:32 did not result in any skin reactions in 6 of 28 Ss. In view of such variations in skin reactions and in the state of cellular immunity, it would seem impossible to explain the onset of subacute sclerosing panencephalitis on the basis of a defect in cellular immunity alone. (5 refs.) - *B. J. Grylack.*

Kanto Teishin Hospital
Tokyo, Japan

1800 **BENNETT, J. S.** Rubella and vaccines: a review of incidence, complications, programs. *Canadian Medical Association Journal*, 106:829-830, 1972.

Rubella, reinstated as a notifiable disease in most Canadian provinces in 1969, is still a significant problem, 101 cases of congenital rubella syndrome being reported to the U.S. National Registry between September 1, 1969, and July 31, 1971. The U.S. Center for Disease Control has received reports of 193 pregnant women who were vaccinated, 171 of whom had unknown immune status prior to vaccination. Of the 56 infants carried to term, 2 had newborn physiologic jaundice, 1 had cystic fibrosis, and 53 were clinically normal at birth. Among provincial vaccination programs there is a variation in the type of vaccine offered and in the population considered at risk. The Canadian Paediatric Society recommends routine immunization of both sexes after the age of 12 months, with emphasis on vaccination of girls prior to puberty; the vaccination of postpubertal females should be preceded by an investigation of immunity status and followed by a satisfactory contraception regime for 3 months postimmunization. - *B. J. Grylack.*

1801 **DAVID, OLIVER; CLARK, JULIAN; &**

VOELLER, KYTJA. Lead and hyperactivity. *Lancet*, 2(7783):900-903, 1972.

Hyperactive children and a nonhyperactive control group were tested for blood lead levels and urine lead levels following oral administration of a single 250mg dose of penicillamine on the preceding evening. The mean blood lead and post-penicillamine urine lead levels were 26.33μg/100ml and 146μg/1, respectively, in the "pure" hyperactive group, and 22.16 μg/100ml and 77μg/1, respectively, in the control group. The group with a "possible" cause for hyperactivity also had significantly raised blood and urine levels, whereas hyperactive children with a "highly probable" cause for hyperactivity had levels not unlike those of the control group. A much higher incidence of a history of lead exposure was found for the hyperactive than for the control children. (12 refs.) - *B. J. Grylack.*

State University of New York
Downstate Medical Center
Brooklyn, New York

1802 MALHERBE, H.; & STRICKLAND-CHOLMLEY, M. Herpesvirus latent in primary rabbit kidney-cell cultures. *Lancet*, 2(7783):930, 1972. (Letter)

A virus which induces changes identical in appearance to those caused by herpesvirus was isolated from uninoculated primary rabbit kidney cells. Syncytia were noted first in a culture bottle which had been observed for 15 days and again 8 days later in other culture bottles from the same tissue batch into which the cells from the first bottle were subinoculated. When cells from these bottles were subinoculated on the fourteenth day into roller tubes containing rabbit kidney coverslip cultures, and when these were stained with hematoxylin and eosin after the fourth day, focal viral changes in the form of large syncytia with nuclear inclusions but no cytoplasmic inclusions were seen. These changes were very similar to the cytopathic effects of some simian herpesvirus strains. (4 refs.) - *B. J. Grylack.*

South African Institute for Medical Research
Johannesburg, South Africa

1803 Fetal/maternal incompatibility. *Lancet*, 2(7784):958-959, 1972. (Editorial)

Since the description in 1957 of a staining technique which could detect small numbers of fetal red cells in adult blood films, research into hemolytic disease of the newborn has progressed significantly. Studies have established that the common episodes of leakage of fetal red cells into the maternal circulation are related to rhesus sensitivity. ABO incompatibility between mother and fetus, long suspected as a cause of spontaneous abortion, may offer some protection against rhesus sensitization. With fetal/maternal ABO incompatibility as common as it is and the placenta constituting a clearly imperfect immunologic barrier, answers must be sought concerning the role of ABO incompatibility and such factors as the HL-A "transplant" antigens and secretor status in abortion and the nature and cause of the apparent immunologic inertia during pregnancy. (22 refs.) - *B. J. Grylack.*

1804 FALORNI, ADRIANO; FRACASSINI, FRANCESCO; MASSI-BENEDETTI, FERDINANDO; & AMICI, AUGUSTO. Glucose metabolism, plasma insulin, and growth hormone secretion in newborn infants with erythroblastosis fetalis compared with normal newborns and those born to diabetic mothers. *Pediatrics*, 49(5):682-693, 1972.

Beta cell reactivity and plasma growth hormone concentration were examined at intervals up to 90 minutes after intravenous injection of 1g glucose/kg body weight in 22 infants with erythroblastosis fetalis (IEF) and were compared with those of 22 normal infants and 12 infants of diabetic mothers (IDM). No significant difference in glucose tolerance (K_t) mean values was found among the 3 groups. During the first 24 hours, the highest fasting mean insulin values were in the IDM group; these infants showed quick and high response to glucose with an insulin secretion pattern different from that in the normal infants, but the rate of glucose removal did not differ significantly from that of the other groups. In general, the insulin curve in IEF was not unlike that of normal SS, but in IEF a significant correlation was found between fasting blood glucose and plasma insulin levels ($p<0.05$), between K_t and plasma insulin values in umbilical vein at 3, 5, and 10 minutes after intravenous glucose injection, added together ($p<0.01$), between hemoglobin and K_t values ($p<0.05$), and between hemoglobin and fasting plasma insulin levels ($p<0.05$). The findings suggested that, while

in IDM factors stimulating pancreatic beta cell activity persisted to some extent for several days after delivery, in IEF the hyperactivity of beta cells was linked to an antagonistic factor, probably established from the relatively recent onset *in utero* and removed abruptly with birth. (34 refs.) - *B. J. Grylack.*

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Universita di Perugia
06100 Perugia, Italy

1805 "Toxemia" of pregnancy. *Canadian Medical Association Journal*, 106:1279-1280, 1972. (Editorial)

The toxemias of pregnancy include the 3 distinct conditions of preeclampsia, defined as the development of hypertension, proteinuria, and edema after the twenty-eighth week of pregnancy; essential hypertension, in which hypertension antedates pregnancy; and chronic renal disease. Clinically, these entities cannot usually be differentiated, and most investigators of preeclampsia have failed to isolate the underlying disease process. "Pure" preeclampsia has been associated occasionally with a bleeding diathesis and with renal failure due to renal cortical necrosis, both complications frequently resulting from disseminated intravascular coagulation. Study of the glomerular lesion presumed to be specific to preeclampsia has provided further support for this association. - *B. J. Grylack.*

1806 **SCOTT, J. S.** Rh-sensitization and third stage of labour. *British Medical Journal*, 2(5809):347, 1972. (Letter)

The value of a recent paper suggesting that rhesus sensitization is to some degree an iatrogenic phenomenon caused by interference with nature's management of the third stage of labor is limited by its lack of orientation to other published work on the subject. Viewed together, all of these studies emphasize the need for assessment of factors influencing fetomaternal hemorrhage in relation to management of the umbilical cord in the third stage of labor on a wider scale than has been carried out up to now. Unfortunately, lack of mention of or reference to another paper on the same subject by an author can seriously impede communication of progress being made. (4 refs.) - *B. J. Grylack.*

University of Leeds
Leeds, England

1807 **UPTON, ADRIAN R. M.** Herpes encephalitis. *British Medical Journal*, 2(5807):226-227, 1972. (Letter)

The results of treatment of herpes simplex encephalitis with idoxuridine and steroids indicate the toxic effect of idoxuridine in most cases, with the mechanism of the therapeutic role played by idoxuridine remaining unclear. The few results of cytarabine treatment in humans are inconclusive, and experimental evidence with animal preparations is even less definitive. If patients are treated with idoxuridine or cytarabine, these measures should be combined with efforts to reduce the intracranial pressure, either surgically or with dexamethasone. In view of the inconclusive data on drugs, it would be premature to dismiss the atraumatic treatment of herpes simplex encephalitis with dexamethasone as unwise. (21 refs.) - *B. J. Grylack.*

McMaster University Medical Centre
Hamilton, Canada

1808 **ZIEGENFUSS, JAY F., JR.** Testing for Australia antigen. *British Medical Journal*, 2(5804):48, 1972. (Letter)

The large number of false positives occurring in fresh serum using the latex agglutination test for the detection of Australia antigen can be eliminated by means of heat inactivation of the sera to be studied at 56° C for 30 minutes. This procedure would also uncover "masked" Australian antigen in certain specimens. (3 refs.) - *B. J. Grylack.*

Abington Memorial Hospital
Abington, Pennsylvania

1809 **SILVERSTEIN, ARTHUR M.** Fetal immune responses in congenital infection. *New England Journal of Medicine*, 286(26):1413-1414, 1972. (Editorial)

The fetal immunological capabilities against various antigens mature at different stages. There are no defenses at first, which permits the devastation of embryonic tissue as in first trimester rubella. Limited competence then develops as in fetal clearance of blue-tongue and lymphocytechoriomeningitis virus in fetal lambs, but some agents persist such as rubella, *Treponema pallidum*, and *Toxoplasma gonadii*. The active fetal immune response may contribute to auto-

immune responses. Specific tolerance can be induced only in an immunologically competent host and is the mechanism preventing reaction against "self-antigens." Tolerance rarely occurs during congenital infection, as circulating IgM antibodies are found in cord blood following congenital infections of rubella, toxoplasmosis, syphilis, and cytomegalovirus. (6 refs.) - *V. J. Goldberg.*

10 Shattuck Street
Boston, Massachusetts 02115

1810 BEHRENDT, HANS; & *GREEN, MARVIN. Nature of the sweating deficit of prematurely born neonates. Observations on babies with the heroin withdrawal syndrome. *New England Journal of Medicine*, 286(26):1376-1378, 1972.

Spontaneous sweating was observed in 30 of 131 healthy full-term (39 wk., 2500g) neonates, 2 of 107 healthy low-weight (27-39 wk; 900-2500g), and 8 of 20 heroin addicted low-weight (27-39 wk, 900-2500g) neonates. Sweating was elicited by 1.0mg/ml epinephrine in 7 of 23 healthy low-weight and 13 of 18 heroin addicted low-weight babies; by 1.0mg/ml acetylcholine in 4 of 26 and 11 of 15 normal and addicted neonates, respectively; and by 0.1mg/ml nicotine in 2 of 15 and 7 of 10 normal and addicted neonates, respectively. Threshold drug effects occurred at much lower concentrations among addicted neonates. The central and glandular components of the sweat mechanism are unresponsive in healthy neonates, but the neural deficit predominates. Sweating could not be elicited in infants of 32 wk gestational age, indicating that glands were not functional at that age. The pathophysiological disturbances of heroin withdrawal may produce an increased toxicity in the sweat centers, providing the innervation for sweat gland activity in the otherwise anhydrotic premature. (8 refs.) - *V. J. Goldberg.*

*Metropolitan Hospital Center
New York, N. Y. 10029

1811 AASE, JON M.; *NOREN, GEORGE R.; REDDY, VENUDHAR; & ST. GEME, JOSEPH W. Mumps-virus infection in pregnant women and the immunologic response of their offspring. *New England Journal of Medicine*, 286(26):1379-1382, 1972.

Twelve children born to 11 Eskimo women who had been exposed to mumps infection were evaluated physically and immunologically 10 yr. after intrauterine contact. No gross abnormalities were found and EKGs were normal. All 9 pre-epidemic controls had positive mumps virus skin test, 8 had neutralizing antibody, and all had a rise in anamnestic antibody (measured 14 days after skin test). Six of 32 post-epidemic controls had positive skin tests, 1 had neutralizing antibody, and 3 had anamnestic response. (The origin of the mump-like antigen was not known). Ten of 12 prenatally exposed children had a positive skin test, none had neutralizing antibody, and 3 had an anamnestic response. The presence of an anamnestic antibody supports the validity of using the delayed cutaneous hypersensitivity as an immunological market for intrauterine mumps infection. (22 refs.) - *V. J. Goldberg.*

Hennepine County General Hospital
Minneapolis, Minnesota 55415

1812 MURPHY, BRIAN R.; KASEL, JULIUS A.; & *CHANOCK, ROBERT M. Association of serum anti-neuraminidase antibody with resistance to influenza in man. *New England Journal of Medicine*, 286(25):1329-1332, 1972.

Volunteers lacking serum or nasal-wash neutralizing antibody to H3 hemagglutinin but with varying levels of serum anti-neuraminidase (ANAB) were inoculated intranasally with $10^5 TCID_{50}$ of influenza A Hong Kong/1968 (H3N2) virus. Illness developed in 10/11 with ANAB titer less than 1:4 and 4/10 with ANAB titer greater than 1:4. Virus particles were recovered from 20/21. The increase in serum or nasal neutralizing antibody titer and the duration of virus shedding were proportional to the severity of the symptoms. These findings indicate that antibodies to both surface antigens have a protective effect. It is possible that ANAB played a role in the 1968-69 flu epidemic. ANAB possibly prevents development and transmission of the disease while antibodies to the virus with an altered hemagglutinin are developed. (16 refs.) - *V. J. Goldberg.*

National Institutes of Health
Bethesda, Maryland 20014

1813 Phototherapy in neonatal jaundice. *British Medical Journal*, 2(5805):62-63, 1972.

Phototherapy for the prevention and management of hyperbilirubinemia in the newborn is being used increasingly but remains controversial. The main uncertainties concern the effects of the photodegradation products of bilirubin and ignorance of its long-term sequelae as well as lack of knowledge as to what concentration of bilirubin in the serum causes neurological damage. Phototherapy has not proved very effective in controlling rapid rises in serum bilirubin, but recent studies indicate its possible usefulness in ABO blood-group incompatibility. The effective alternatives to phototherapy, among them exchange transfusion, phenobarbitone and other enzyme inducers, orotic acid, and agar, carry with them a certain risk. (32 refs.) - *B. J. Grylack.*

1814 **HIERHOLZER, JOHN C.; MOSTOW, STEVEN R.; & DOWDLE, WALTER R.** Prospective study of a mixed Coxsackie virus B3 and B4 outbreak of upper respiratory illness in a children's home. *Pediatrics*, 49(5):744-752, 1972.

A discrete outbreak of moderately severe upper respiratory illness associated with Coxsackie virus types B3 and B4 was studied in 120 children (CA 3 to 19 years) residing in a children's home. Seventy-three percent of reported B3 illnesses and 83% of reported B4 illnesses were upper respiratory. A stronger association was found between B3 and conjunctivitis, exudative tonsillopharyngitis, otitis, and exanthem than between B4 and these symptoms. Isolation rates from throat swabs taken from B3-associated illnesses (62%) and B4 illnesses (42%) and from eye swabs from children with conjunctivitis (43%) were unusually high. A clear correlation was found between infection and CA, all Ss in the 0 to 4 year age group but only 23% in the >16 group being infected. Preexisting antibody at serum neutralization levels of 1:20 or greater provided complete protection against reinfection by B3 or B4. Double infections (all sequential) were rare with the exception of a 7-year-old girl, in whom the relationship between delayed antibody response and persistent virus shedding from the throat was unclear. The clinical illness and subclinical infection rates were 22% and 19%, respectively, for B3, and 10% and 21%, respectively, for B4. (23 refs.) - *B. J. Grylack.*

Public Health Service
U.S. Department of HEW
Atlanta, Georgia 30333

1815 **DOWDLE, WALTER R.** Influenza antineuraminidase: the second best antibody. *New England Journal of Medicine*, 286(25):1360-1361, 1972. (Editorial)

The influenza virus has 4 major structural proteins, but the antibodies against the 2 surface antigens, hemagglutinin and neuraminidase, are of interest in protection from disease. The hemagglutinin spikes are more numerous on the virus surface and appear to attach the virus to the cell receptors. The neuraminidase spikes are less than 1/3 as frequent and may function either to release newly formed virus particles from the host cell membrane or to degrade the cell membrane for virus access. Serum neuraminidase antibodies may relate to protection or indicate subdetectable antibody levels in secretions. The neuraminidase antigen is probably not the active enzyme site; therefore it is unlikely that interaction with the antibody completely inhibits enzyme activity. The 1968-69 flu pandemic was caused by a virus with antigenic changes in the hemagglutinin, but changes in both viral surface antigens may have resulted in a more severe epidemic as was the case in 1957. Both surface antigens should be measured for vaccine formulation. (5 refs). - *V.J. Goldberg.*

1816 **CZEIZEL, A.** Influenza and infant mortality. *British Medical Journal*, 3(5837):430, 1972. (Letter)

The birthweights of babies of women who had had influenza during the last months of pregnancy were lower (< 2,500g) than those of unaffected women in about 5% of cases in a Hungarian study, and a decrease in live births was also demonstrated 9 months after influenza epidemics. However, no correlation was noted between the monthly stillbirth rate or the rate of spontaneous abortions and the peak months of influenza epidemics from 1950 to 1965. (2 refs.) - *B. J. Grylack.*

National Institute of Public
Health
Budapest, Hungary

1817 **DODGE, J. S.** Vaccination against rubella. *British Medical Journal*, 2(5810):407, 1972. (Letter)

Immunization of children of both sexes against rubella before they attend school or kindergarten would produce an immune population in the groups which were previously most susceptible to

rubella infection and were the main vehicles of the spread of the disease to pregnant women. An advantage of this method of protection is that reactions to the vaccine are usually less among children in the age range 4 to 5 years than among those aged 11 to 14 years. If the vaccine proved to produce a long, perhaps lifelong period of immunity, then adults would be protected directly as well as indirectly. - *B. J. Grylack.*

University of Otago
Dunedin, New Zealand

1818 **CARRELLA, M.; DEL VECCHIO-BLANCO, C.; & COLTORTI, M.** Australia antigen in chronic liver disease. *British Medical Journal*, 2(5806):168-169, 1972. (Letter)

Investigation of 126 cases of chronic liver disease, confirmed by biopsy, from a population with a high incidence of cryptogenic and posthepatic cirrhosis compared with alcoholic cirrhosis showed a very high incidence of Australia antigen in chronic aggressive hepatitis, both with complement fixation and immunodiffusion in agarose, compared with a relatively low frequency in chronic persistent hepatitis and a high incidence in cases of posthepatitis and cryptogenic cirrhosis as well. The reasons for these findings are unclear. (2 refs.) - *B. J. Grylack.*

University of Naples
Naples, Italy

1819 **BEATTIE, A. D.; DAGG, J. H.; GOLDBERG, A.; WANG, I.; & RONALD, J.** Lead poisoning in rural Scotland. *British Medical Journal*, 2(5812):488-492, 1972.

Four families living in rural parts of the Scottish Highlands had lead intoxication acquired from contamination of the domestic water supply. Of 20 Ss tested in the 4 families, 9 were found to have clinical or biochemical evidence of lead intoxication, 5 showing symptoms of lead poisoning and the other 4 manifesting unequivocal biochemical evidence of excessive lead exposure. Seven of 11 patients tested had hyperuricemia. Removal of all the lead plumbing from the house occupied by 1 family and replacement of lead piping in the house occupied by a second family resulted principally in a fall in the level of erythrocyte protoporphyrin. - *B. J. Grylack.*

M.R.C. Group in Iron and
Porphyrin Metabolism
Stobhill Hospital
Glasgow, Scotland

1820 **HERISHANU, Y.; MAZAL, S.; & LAVY, S.** Hyperbilirubinemia in acute haemorrhagic stroke. *Journal of the Neurological Sciences*, 17(4):369-372, 1972.

Serum bilirubin levels were studied in 24 patients with acute hemorrhagic stroke to determine whether hepatic changes are affected by this intracranial pathology. The total bilirubin values ranged between 0.1 and 2.4mg/100ml; normal levels (0.1-1.1) were found in 13 patients and levels above 1.1mg/100ml in 11 patients (45.8%). The high values were found in the first 5 days after the stroke. The parallel rise in plasma of direct and total bilirubin in the hemorrhagic stroke patient, in which a follow-up showed continued above-normal bilirubin levels, suggests the possibility that intracranial pathology and intracranial pressure act together to cause changes in hepatic cell polarity, so that direct bilirubin is secreted into the plasma instead of into the biliary capillaries. (14 refs.) - *A. C. Schenker.*

Hadassa University Hospital
Jerusalem, Israel

1821 **FERRENDELLI, JAMES A.; & CHANG, MING-MING.** Brain metabolism during hypoglycemia. *Archives of Neurology*, 28(3):173-177, 1973.

The effect of insulin hypoglycemia on glucose and high energy phosphate reserves in several regions of mouse brain was studied in adult, Swiss-Webster mice of both sexes. Following insulin treatment, the animals developed a consistent clinical syndrome: within 15-30 min they became lethargic but responded appropriately to stimuli; within 30-75 min, intermittent myoclonic and clonic seizure activity was observed until the animals lost their righting reflex and became stuporous, between 40-120 min. The clinical signs exhibited by the hypoglycemic animals indicate depression of neural function beginning in higher levels and progressing to lower levels of the central nervous system (CNS). The finding of a uniform decrease of glucose reserves and a uniform depression of

high-energy phosphate utilization throughout the CNS during hypoglycemia does not support the thesis that the clinical signs are a result of a progressive rostal-caudal depletion of glucose reserves or depression of high-energy phosphate use. The findings indicate that blood glucose levels probably cannot be used to estimate CNS metabolic derangement in hypoglycemic patients. (18 refs.) - *A. C. Schenker.*

Washington University School of Medicine
St. Louis, Missouri 63110

1822 Viral heptitis. *British Medical Journal*, 1(5815):669-670, 1972.

From the 1940's, when the short-incubation form, or infectious hepatitis, was distinguished from the long-incubation form, or serum hepatitis, little progress was made in viral hepatitis until 1964, when the discovery of Australia antigen caused a dramatic change. This discovery was followed by reports of a different serum antigen, the Milan or epidemic-hepatitis-associated antigen, but the evidence suggests that this antigen is probably an abnormal serum lipoprotein which appears as the result of liver damage due to various causes and is not associated specifically with infectious hepatitis. Screening of blood for transfusion for the presence of Australia antigen has remained of great importance. (4 refs.) - *B. J. Grylack.*

1823 LOWENTHAL, A.; MOYA, G.; POIRE, R.; MACKEN, J.; & DE SMEDT, R. Subacute sclerosing panencephalitis: a clinical and biological reappraisal. *Journal of the Neurological Sciences*, 15(3):267-270, 1972.

A review of the clinical and biological features of 6 typical cases of subacute sclerosing panencephalitis (SSPE) is presented. Chronic cases of this disease have been noted in older children and young adolescents in which the onset of the illness is similar to the classical descriptions. Apart from dificulty with speech, dysphagia, and visual failure, there are few signs of damage to the cranial nerves. The evolution is slow, sometimes interrupted by intervals of months and years. In all the specimens of cerebral spinal fluid (CSF), the level of gammaglobulin was increased; in 80% of the sera there are M components of the gamma-globulin. In 9 CSF and 18 serum specimens, increased measles antibody titres were present. It is clear that SSPE can develop in young adults. (12 refs.) - *A. C. Schenker.*

Institute Bunge
Berchem-Antwerp, Belgium

1824 CAPE, CHARLES A.; MARTINEZ, A. JULIO; ROBERTSON, JAMES T.; HAMILTON, REBECCA; & JABBOUR, J. T. Adult onset of subacute sclerosing panencephalitis. *Archives of Neurology*, 28(2):124-127, 1973.

An adult case of subacute sclerosing panencephalitis (SSPE) is described, which is believed to be the first such case in which the relationship to measles has been established. The patient was a 32-year-old man who was hospitalized with a 2-month history of visual loss and of abnormal behavior. On admission he was demented and had periodic myoclonic seizures. The man's condition deteriorated and he died 8 months after the onset of the illness. A right occipital brain biopsy, performed 3 months after the onset of his illness, and postmortem examination showed glial cells with intracytoplasmic inclusion in the left occipital lobe, and membranous bound inclusion with irregular filamentous tubular structures in the right occipital lobe, consistent with paramyxovirus nucleocapsids. Fluorescent antibody assays, performed with the patient's serum and paired human measles sera, evidenced foci of specific immunofluorescence in the brain tissue culture. Cultures were freeze-thawed twice and virus suspension obtained from them neutralized by serial dilutions of SSPE and normal serum samples; the hemagglutination activity of this isolate was specifically blocked by measles antisera. (12 refs.) - *A. C. Schenker.*

University of Tennessee
Memphis, Tennessee 38103

1825 TOULOUKIAN, ROBERT J.; KADAR, ANDREW; & SPENCER, RICHARD P. The gastrointestinal complications of neonatal umbilical venous exchange transfusion: a clinical and experimental study. *Pediatrics*, 51(1):36-43, 1973.

A study of 2 newborn infants with gastrointestinal complications following exchange transfusion and review of 21 previously reported cases showing an association of neonatal umbilical venous exchange transfusion with subsequent gastrointestinal,

primarily colonic, perforation has indicated a prevalence of abdominal distention, gastric retention, or bilious vomiting and blood-streaked or bloody stools prior to the onset of these complications. An experimental investigation designed to determine whether the umbilical venous catheter is the source of hemodynamic, embolic, or septic complications which could produce gastrointestinal lesions in the newborn piglet showed a significant increase in portal venous pressure during the injection phase of exchange. The evidence suggested a vascular mechanism, possibly producing mucosal ischemia secondary to venous congestion. The data stressed the need to perform exchange transfusions with a radioopaque catheter or a test injection of a contrast agent used to visualize the position of the clear plastic catheter available on the standard exchange transfusion tray. (23 refs.) - *B. J. Grylack.*

Yale University School of Medicine
New Haven, Connecticut 06510

1826 ALTAY, CIGDEM; & *SAY, BURHAN. Phototherapy in nonobstructive, nonhemolytic jaundice. *Pediatrics*, 51(1):124-126, 1973.

A male infant with Crigler-Najjar syndrome, presumably Arias type I, was treated successfully with phototherapy. Despite continuous light therapy, the bilirubin level did not fall below the 10mg/100ml level. During the first few months serum bilirubin levels were maintained at 10 to 12 mg/100 ml with 16 hours' daily treatment with 4 40-watt bulbs, but levels ranged from 16 to 17mg/100ml around the age of 6 months. The data indicated that rising total plasma volume and hemoglobin values, increasing skin thickness, and pigmentation may be causative factors in decreasing light effectiveness and that increased light power may be required to maintain bilirubin at safer levels. The case demonstrated that the products of photolysis of bilirubin are not toxic even when an infant is subjected to them for many months. (12 refs.) - *B. J. Grylack.*

*Hacettepe University
Hacettepe, Ankara, Turkey

1827 HANSON, L. A.; HOLMGREN, J.; JODAL, U.; LINCOLN, K.; & LINDBERG, U. Asymptomatic bacteriuria--a serious disease? *British Medical Journal*, 2(5812):530, 1972. (Letter)

The findings from studies of urinary tract infections in children with asymptomatic bacteriuria suggest that asymptomatic bacteriuria may be considered a potentially dangerous disease in many cases and not a harmless invasion of the urinary tract, even though the bacteriuria has disappeared spontaneously in some of these cases. The data indicate that asymptomatic bacteriuria occurs primarily in patients who have had previous attacks of urinary tract infections. More than 15% of the children with asymptomatic bacteriuria showed signs of renal damage, which is probably a sequel of urinary tract infections. (6 refs.)- *B. J. Grylack.*

University of Goteborg
Goteborg, Sweden

1828 RAPPEL, MARC. Herpes encephalitis revisited. *British Medical Journal*, 2(5814):655-656, 1972. (Letter)

Retrospective examination of 369 cases of acute necrotizing encephalitis either published in the world literature or comprising the subject of personal communications suggests that any treatment is better than no treatment at all. Among the various therapeutic regimens used, however, there is no valid evidence that any one treatment is superior to the others. It is important to point out that the use of steroids alone seems to be hazardous, and dexamethasone should always be used in combination with antiviral chemotherapy if it is to be used at all. (11 refs.) - *B. J. Grylack.*

Universite Libre de Bruxelles
Brussels, Belgium

1829 HARTE, JOHN D. Vaccination against rubella. *British Medical Journal*, 1(5801):689, 1972. (Letter)

Results of rubella immunization of high-risk nonpregnant hospital staff in 1970 and 1971 indicate the unreliability of a history of rubella. Of 135 individuals tested in 1971, 2 of 43 women with a definite history of rubella were susceptible, and 41 were immune, while 25 of 92 with no history of rubella were susceptible, and 67 were immune. - *B. J. Grylack.*

Staff Occupational Health
Department
Bedford General Hospital
Bedford, England

1830 **ANAND, J. K.; POOLEY, JOAN M.; & WHITE, W. D.** Vaccination against rubella. *British Medical Journal*, 1(5796):375, 1972. (Letter)

In an effort to identify and immunize seronegative women at risk belonging to certain special groups, the school health service in the London (England) borough of Redbridge has announced that it will willingly provide rubella vaccine to general practitioners in order to immunize the female school teachers at risk. The current policy of careful serologic testing during the early antenatal period of any pregnant woman at risk from contact is also strongly supported, and follow-up and retesting after a 4-week interval of women whose serum shows absence of or a very low titer of antibodies are encouraged. - *B. J. Grylack.*

London Borough of Redbridge
England

1831 **MELDRUM, B. S.** Childhood hypoglycaemia. *British Medical Journal*, 1(5796):379, 1972. (Letter)

Childhood hypoglycemia is important as a possible cause of brain damage. Studies of profound hypoglycemia in primates indicated that all animals developing brain damage had experienced blood glucose levels below 20mg/100ml for 2 to 10 hours but that hypoglycemia of this severity could last from 3 to 5 hours without producing brain damage. Experimentation with adult animals showed that all cases subsequently manifesting brain damage had experienced periods of profound central nervous system depression. While convulsions may be a symptom of hypoglycemia, hypoglycemia is also possible as a secondary feature of prolonged seizures. (8 refs.) - *B. J. Grylack.*

M.R.C. Neuropsychiatry Unit
Carshalton, Surrey, England

1832 **LINK, HANS; PANELIUS, MARTIN; & SALMI, AINO A.** Immunoglobulins and measles antibodies in subacute sclerosing panencephalitis: demonstration of synthesis of oligoclonal IgG with measles antibody activity within the central nervous system. *Archives of Neurology*, 28(1):23-30, 1973.

Immunoglobulins and complement factors in serum and CSF were evaluated quantitatively in patients with subacute sclerosing panencephalitis (SSPE), and the immunoglobulin levels were analyzed in relation to the antibody levels against different structural components of measles virus. CSF and serum samples were obtained from 8 patients with SSPE and from 8 healthy controls. Samples were assayed for IgG, IgA, IgM, βC/βA globulins, βE globulin, and for type K and type L light chain antigenic determinants. Increased gamma-globulin concentration of the CSF in SSPE was found and attributed to a selective increase in IgG. The CSF and serum findings in SSPE showed: increased total protein concentrations in CSF, increased CSF/IgG, normal CSF/IgA, and probably normal CSF/IgM concentrations when expressed in percent of the total protein concentrations of CSF, normal CSF concentrations of βC/βA globulins and of βE globulin, increased CSF type K: type L ratios and normal serum type K: type L ratios, and abnormal patterns on agar gel electrophoresis. Synthesis of oligoclonal IgG with measles antibody activity within the CNS was observed in SSPE. (33 refs.) - *A. C. Schenker.*

University Hospital
Lund, Sweden

1833 **CAPPEL, ROGER; & KLASTERSKY, JEAN.** Herpetic meningitis (type 1) in a case of acute leukemia. *Archives of Neurology*, 28(6):415-416, 1973.

The association of hematological malignancies and viral disorders of the CNS is illustrated in a case of meningitis caused by herpes simplex virus (HSV) type 1, which occurred in a 23-year-old man with acute lymphoblastic leukemia. HSV was identified in his cerebrospinal fluid, and complement fixing reaction on samples of serum demonstrated a rise in the titer of antibody to HSV from less than 1/2 to 1/22. The patient died on the seventh day from leukemia. No pathological abnormalities could be found at autopsy just a few days after the onset of neurological symptoms. However, in patients with severe granulocytopenia, the clinical and pathological signs of infection may be inconspicuous. (11 refs.) - *A. C. Schenker.*

Institut Jules Bordet
1000 Brussels, Belgium

1834 **PANITCH, HILLEL S.; & *BARINGER, J. RICHARD.** Experimental herpes simplex encephalitis: treatment with pyrimidine

nucleosides. *Archives of Neurology*, 28(6):371-375, 1973.

The effect of idoxuridine and cytarabine on the development of histological lesions in an experimental model of herpes simplex encephalitis was investigated. New Zealand white rabbits were infected by means of unilateral corneal scarification and installation of one drop of the Rodanus strain of herpes simplex virus into the conjunctival sac. Groups of animals were treated with either idoxuridine (300mg/kg/day for 5 days) or cytarabine (40mg/kg/day for 3 days) which was initiated 3 days after corneal infection. Animals infected and treated with idoxuridine all developed lesions similar to those seen in untreated animals. In animals treated with cytarabine, brainstem lesions developed in only 8 of 13 animals and in all the untreated animals. In the other 5 treated animals, the lesions were very small with little inflammatory reaction or hemorrhage, and only 1 treated rabbit showed evidence of cerebral infection. However, when a second group of animals, treated with cytarabine, was permitted to survive 8 days (instead of 3), the lesions developed as in controls. Thus, cytarabine appeared to retard the development of histological lesions produced by herpes simplex virus, whereas idoxuridine appeared ineffective. (43 refs.) - *A. C. Schenker*.

Veterans Administration Hospital
San Francisco, California 94121

1835 **WEINER, LESLIE P.** Pathogenesis of demyelination induced by a mouse hepatitis virus (JHM virus). *Archives of Neurology*, 28(5):298-303, 1973.

The pathogenesis of JHM virus infections of mice was studied to determine the cellular localization of virus replication, to confirm the demyelinative nature of the lesions, and to evaluate the possible role of immune responses or hepatic disease. Outbred Swiss mice were used. The animals had no antibody for mouse hepatitis virus and were used immediately upon arrival. The development of demyelinative lesions with JHM virus infection was dependent on age, dose, and route of inoculation. A preferential infection of glial cells of white matter was demonstrated. Lesions were most prominent in gray matter of the olfactory bulb, hippocampus, and quadrigeminal region and in white matter of the pons, corpus callosum, hippocampal commissure, internal capsule, and spinal cord. Occasional giant cells were seen within the demyelinative lesions in mice induced by JHM virus; these appeared to be composed of inflammatory cells. Six of 9 animals inoculated with JHM virus antiserum and 10 $SMLD_{50}$ virus showed demyelination with no evidence of hepatic disease. Evidence of any immunopathologic process in viral-induced demyelination could not be demonstrated. (20 refs.) - *A. C. Schenker*.

Johns Hopkins School of Medicine
Baltimore, Maryland 21205

1836 **SCHWARTZ, JEROME; & *ELIZAN, TERESITA S.** Chronic herpes simplex virus infection: initiation in hamsters upon implantation of infected nonpermissive glial cells. *Archives of Neurology*, 28(4):224-230, 1973.

Variable response of several transformed glial and neuronal cell lines to infection with herpes simplex virus (HSV), the nonpermissive nature of one glial response, and the initiation of a chronic HSV infection in hamsters upon implantation of these transformed, infected nonpermissive glial cells, are described. The general aim of the project is to study the latent phase of HSV in an affected host and the factors which then permit initiation of a virulent phase of infection. The response of cells in tissue culture to HSV infection is seen to range from nonpermissive to completely permissive for virus production. The studies show that in order for infectious virus to be produced, the nuclear membrane must become extensively altered. In completely permissive cells (e.g. HEp-2 or IMR-32) the nuclear membrane provides an envelope for nucleocapsids and the expanded perinuclear space provides a compartment for the accumulation of enveloped particles. In the C-6 astrocyte cell line, no envelopment of nucleocapsids occurs and little or no infectious virus is made. The capacity of infected nonpermissive C-6 cells to initiate a chronic herpes infection in hamsters indicates that infectious virus can be rescued from the nonpermissive cells at low levels; this cell type is particularly valuable for experimental studies. (37 refs.) - *A. C. Schenker*.

*Mount Sinai School of Medicine
New York, New York 10029

1837 **GONYEA, EDWARD F.** Cisternal puncture and cryptococcal meningitis. *Archives of Neurology*, 28(3):200-201, 1973.

Positive cultures of Cryptococcus neoformans, obtained from cerebrospinal fluid (CSF) from a cisternal puncture, are reported in 2 cases. These cases represent the first documented account of lumbar CSF culture-negative cryptococcal meningitis being diagnosed by the culture of Cryptococcus neoformans from CSF obtained from cisternal puncture. Positive india-ink preparations and cultures from ventricular and cisternal, but not lumbar, CSF suggest that there is a differential concentration gradient of organisms in the various CSF regions which should be taken into account in making a diagnosis. (7 refs.) - *A. C. Schenker.*

Neurology Service
Veterans Administration Hospital
Gainesville, Florida 32601

1838 **HANISSIAN, ARAM S.; MARTINEZ, A. JULIO; JABBOUR, J. T.; & DUENAS, DANILO A.** Vasculitis and myositis secondary to rubella vaccination. *Archives of Neurology*, 28(3):202-204, 1973.

An acute reaction to rubella vaccine is described in a 6-year-old boy immunized with live, attenuated rubella virus vaccine (Meruvax Duck Cell). The child developed a low grade fever and a maculopapular exanthematous rash 2 days later. The fever (98 to 105 F) responded partially to salicylates and to prednisone. Hematological examination was conducted and muscle biopsies were examined by both light and electron microscopy. A generalized Arthus' reaction or serum sickness reaction was suggested by the reticuloendothelial hyperplasia, eosinophilia, leukocytosis, vasculitis, and neuritis. The severity of the reaction was attributed to an immunopathologic reaction. (8 refs.) - *A. C. Schenker.*

University of Tennessee College of Medicine
Memphis, Tennessee 38103

1839 **NADJI, POURAN; & SOMMERS, SHELDON C.** Lesions of toxemia in first trimester pregnancies. *American Journal of Clinical Pathology*, 59(4):344-349, 1973.

Histologic material from 326 induced abortions is described in connection with the etiology of toxemia of pregnancy. The microscopic slides were reviewed without knowledge of the clinical state and the 2 recognized lesions associated with toxemia of pregnancy, decidual arterial thickening and narrowing and degenerated chorionic villi were sought. Both of these lesions were found in 46 of the cases. The observations of preclinical toxemia of pregnancy support the intrauterine origin of the process. The major distinctive difference in toxemia is the endothelial lipid vacuolization (acute atheroma). The decidual vascular changes are sufficient to produce ischemia of the decidua and adversely affect the placenta. With regard to the state of pregnancy, parity, physical examination, and laboratory findings, no difference was found between the women with and without the intrauterine changes of toxemia. (12 refs.) - *A. C. Schenker.*

Lenox Hill Hospital
New York, New York 10021

1840 Case records of the Massachusetts General Hospital: weekly clinicopathological exercises: presentation of a case. *New England Journal of Medicine*, 288(7):363-367, 1973.

In a clinical pathological conference, a newborn infant with a tentative diagnosis of maternal and fetal infection with rubella or cytomegalic inclusion disease (CID) is described; intrauterine growth retardation was associated with the latter. The 3 salient features of the case of the infant, who weighed 1.8kg at birth and who died on the fifth day of hospital admission, were the marked intrauterine growth retardation, a question of disseminated intravascular coagulation (DIC) as evidenced by major bleeding, and depression of the megakaryocytes found in the bone-marrow examination. Four infections were considered in the diagnosis, all potentially teratogenic. Postmortem examination revealed inclusion bodies in a number of organs. Dissecting tracts of blood and marked gliosis were seen in the brain, but no well developed inclusions. The relation between CID and DIC is of interest, since several clinical studies of CID have documented the presence of petechiae (also extensively seen in this infant), purpura, and thrombocytopenia, suggesting that CID may have a hemolytic component. The anatomical diagnosis was cytomegalic inclusion disease with disseminated intravascular coagulation. The question of when cytomegalovirus infection may be called a disease is considered. (12 refs.) - *A. C. Schenker.*

1841 **DIAMOND, RICHARD D.; & BENNETT, JOHN E.** A subcutaneous reservoir for intrathecal therapy of fungal meningitis.

New England Journal of Medicine, 288(4):186-188, 1973.

Complications related to intrathecal therapy of fungal meningitis are described in 10 of 21 patients in whom reservoir insertion presented problems and in cases reported by others. Over the past 10 years, 31 subcutaneous reservoirs have been placed in 21 patients to provide a direct route for injection of amphotericin B into cerebrospinal fluid. Of the 10 patients with complications, 4 had catheter tips ending in the third ventricle and all experienced severe toxic reactions to the antibiotic. The severe problems encountered with amphotericin B injections into the third ventricle suggest the importance of early radioisotope ventriculography or pneumoencephalography to establish catheter position definitely. Shunts also contributed to therapeutic failure by rapidly draining the injected antibiotic out of the cerebrospinal fluid. Because of the high morbidity and the absence of more extensive evidence for efficacy, it is suggested that intraventricular therapy in cryptococcal meningitis be reserved for patients who relapse or fail to respond to i.v. amphotericin B, and for those whose toxic reactions to such therapy preclude the use of adequate i.v. doses. (14 refs.) - *A. C. Schenker.*

National Institute of Allergy
Bethesda, Maryland 20014

1842 MILLMAN, I.; LONDON, W. THOMAS; & BLUMBERG, B. S. Immunofluorescent identification of Australian antigen. *New England Journal of Medicine*, 288(2):108-109, 1973. (Letter)

In reference to comments by Beccati, Fabris, and Nenci regarding the fluorescent antibody technique reported, which they claim to be nonspecific, further evidence is presented to support the specificity of this test. Whereas Beccati et al. found no relation between fluorescence and clinical and histologic changes or Australia antigen (Au) in the serum, in the study reported significant associations were found between nuclear fluorescence and Au in the serum and between histologic evidence of hepatitis and nuclear fluorescence, the chi squares being 19.58 and 16.05, respectively ($p<0.001$). It was shown by simultaneous phase microscopy that the fluorescent bodies were not associated with the nucleolus. Furthermore, electron microscopic studies by others have shown that intranuclear localization of Au particles is the primary ultrastructural form of Au and that the nucleus of the hepatocyte is its primary cellular site. (7 refs.) - *A. C. Schenker.*

Institute for Cancer Research
Fox Chase
Philadelphia, Pennsylvania

1843 FINBERG, LAURENCE; & ROSEN, JOHN F. Lead in "No-lead" paint. *New England Journal of Medicine*, 288(7):876, 1973. (Letter)

The discovery of lead in vinyl acrylic paint labeled "No lead" is reported. Samples of the paint were allowed to stand in 2ml of either hydrochloric or nitric acid at a pH of 3 or 4. After 15 minutes, the samples were centrifuged and aliquots of the supernatant were analyzed for lead. From 4 to 6 μgm lead/gm of paint was extracted. - *A. C. Schenker.*

Montefiore Hospital and Medical Center
Bronx, New York

1844 NEEDLEMAN, HERBERT L.; & SCANLON, JOHN. Getting the lead out. *New England Journal of Medicine*, 288(9):466-467, 1973.

The toxic effects of lead, especially for children, are outlined and steps to remove these hazards are urged. Ambient air lead levels have increased steadily in this country in direct proportion to the number of automobiles on the road. Blood lead levels of individuals exposed to airborne lead are substantially higher than those of workers in other occupations. Urban residents have higher lead levels than suburban residents; this is particularly hazardous for children. Examination of the home of lead poisoned children in New York City revealed that one home out of 4 did not have peeling paint surfaces, suggesting another source of lead poisoning. The standards applied to healthy male adults cannot be generalized to include all sectors of the population. Studies in lead poisoning which determine precise dose response must be done. Enough data are at hand to establish that this metal of known toxicity is being issued into the human environment; the removal of lead from contaminating sources, including gasoline, must be effected without delay. (10 refs.) - *A. C. Schenker.*

1845 BARINGER, J. RICHARD; & SWOVELAND, PEGGY. Recovery of herpes-

simplex virus from human trigeminal ganglions. *New England Journal of Medicine*, 288(13):648-650, 1973.

The recovery of herpes-simplex virus from human trigeminal ganglions in routine autopsy material is reported and the results of the tissue culture, fluorescence, and electron microscopic study of 7 patients tabulated. Moderate outgrowth of cells was obtained from all cultured ganglions and nerve. After varying periods in culture, ganglions from 6 patients exhibited a cytopathic effect typical of that produced by herpes-simplex virus. When selected nerve or root cultures were deliberately infected with the virus obtained from the ganglion cultures, a viral cytopathic effect was produced. The recovery of the virus only from the ganglions and not from adjacent nerve or root in this series suggests that the virus may reside within ganglion cells. (34 refs.) - *A. C. Schenker.*

Veterans Administration Hospital
San Francisco, California 94121

1846 **TRIPODI, D.; HAWK, J.; GOCKE, D. J.; REDEKER, A.; & STARKOVSKY, N. A.** Detection of antibody to hepatitis-associated antigen by indirect counterimmunoelectrophoresis. *American Journal of Clinical Pathology*, 59(4):549-551, 1973.

A modification of the counterimmunoelectrophoresis (CEP) method whereby the migration of antigen is inhibited by antibody is described; it is a simple, rapid, and sensitive method for detecting anti-hepatitis associated antigen (anti-HAA). The standard anti-HAA used in the studies was a rabbit anti-HAA; a strong HAA-positive which titered 1:64 by CEP and a weaker antigen preparation were used. Double diffusion was capable of detecting 6 of 41 (14.6%) of anti-HAA; direct CEP detected 16 of 39 (41%); and indirect CEP detected 39 of 41 (95.3%) anti-HAA. All 20 control negative sera were negative. (6 refs.) - *A. C. Schenker.*

Ortho Research Foundation
Raritan, New Jersey

1847 **KLOCK, LAWRENCE E.; & RACHELEFSKY, GARY.** Failure of rubella herd immunity during an epidemic. *New England Journal of Medicine*, 288(2):69-72, 1973.

The epidemiologic characteristics of a rubella epidemic and the implications of its occurring in the presence of herd immunity in young children is discussed. Over 1,000 cases of rubella occurred in Casper, Wyoming, in the first 4 months of 1971, of which 84% were in 12- to 18-year-old individuals. Rubella control in the United States is based on the concept of herd immunity, in which the proportion of immune members is large enough to reduce the probability of infection in the susceptible members of the population. The occurrence of this epidemic is considered to have been due to the failure of the herd immunity as it applies to rubella control. Immunity in one segment of the population may have no influence on the occurrence of this disease in a second segment of that population. The most important consequence of such an occurrence is the realization that rubella control must be applied to nonpregnant women in the childbearing age. (10 refs). - *A. C. Schenker.*

U. S. Department of Health,
Education and Welfare
Atlanta, Georgia 30333

1848 **WEINSTEIN, LOUIS; & CHANG, TE-WEN.** Rubella immunization. *New England Journal of Medicine*, 288(2):100-101, 1973.

Failure of herd immunity with regard to rubella is discussed and the factors responsible for this failure are contrasted with those which contribute to successful herd immunity in poliomyelitis. One striking difference is the nature of the infectious agent, one being an entovirus and the other a togavirus. The mode of transmission and acquisition is another factor; rubella is transmitted via the respiratory tract and poliomyelitis via the ingestion of contaminated water or food. The nature of the vaccine strain and its behavior after administration may play an important role in the extent of the immunity. Dissemination of the vaccine strains of rubella virus from immunized to unimmunized persons is rare, unlike attenuated poliomyelitis virus. It is clear that the concept of herd immunity and its role in protection of the unimmunized against rubella is no longer tenable. Immunization against rubella must be concentrated in prepubertal girls and in women known to be nonimmune immediately after delivery of a child. (4 refs.) - *A. C. Schenker.*

1849 RUBIN, ROBERT J. Vaccination for influenza. *New England Journal of Medicine*, 288(10):525,1973. (Letter)

Points raised by Dr. Beekman regarding the outbreak of influenza at Fort Huachuca are commented upon. The fact that B Massachusetts/3/66 was incorporated into the vaccine used by Dr. Beekman suggests that he was using last year's vaccine; this year's contains 700 CC AU of the type A antigen, whereas last year's contained a smaller number of CC AU. The Center for Disease Control supported Dr. Beekman only in identification of the virus, not in the epidemiologic study he reports. The Center for Disease Control and the World Influenza Center in London suggest that the vaccine currently available produces hemagglutination-inhibition titers of greater than 1:20 against A England 42 72. The currently available influenza vaccine is believed to offer some protection against the newer strains. - *A. C. Schenker.*

Center for Disease Control
Atlanta, Georgia

1850 FEEMAN, WILLIAM E., JR. Clinical rubella after reinfection (cont.). *New England Journal of Medicine*, 288(10):525, 1973.

Pertinent questions are asked regarding the case of rubella infection in pregnancy described by Haukenes and Haram. At what stage of her pregnancy did the woman contract rubella? Was the child affected clinically? Was the child affected biochemically as indicated by IgG and IgM determinations? If the answers to these questions are indicative of *in utero* infection, all women planning a pregnancy should have their rubella hemagglutination-inhibition titer checked; if it is sufficiently low they should be reimmunized before conception. - *A. C. Schenker.*

USAF Hospital, RAFL
New York

1851 BELL, T. M.; CASPARY, E. A.; COWSHALL, SHIRLEY; FIELD, E. J.; NARANG. H. K.; & *NOBLE, T. C. Measles virus associated with an unusual subacute encephalitis in an infant. *Journal of the Neurological Sciences*, 16(4):455-463, 1972.

The isolation of a strain of measles virus from the brain of a child suffering from subacute encephalitis is reported, and evidence is presented to suggest that the infection was acquired *in utero*. Morphological and immunological characters of measles virus were found in a biopsy specimen of the brain of a 14-month-old child; the implication of measles virus in the etiology of her illness was supported by the low measles sensitization of the child's lymphocytes to measles antigen and the very high antibody level in the mother. The virus was recovered from the biopsy both by cocultivation with monolayers of LLC-MK_2 cells and following culture of the biopsy tissue itself. It is suggested that other obscure cases of encephalitis in infants might be studied for lymphocyte sensitization to common viruses and that this might be a better indication of infection under these conditions than the level of circulating antibody. (21 refs.) - *A. C. Schenker.*

Newcastle upon Tyne NE4 6BE
England

1852 TERRENATO, L. Beta- and non-beta-thalassaemia in Sardinia and their frequencies. *Annals of Human Genetics*, 36(2):285-295, 1973.

HB A_2 technique and standard hematological procedures were used to detect thalassemia syndromes in Sardinia; the population comprised 233 random Ss, 69 of whom were Ss related (fathers or uncles) to Cooley babies. Screening for G-6-PD deficiency was included. All the Ss showed a normal hemoglobin electrophoretic pattern and 59 out of the 302 Ss proved to be Gd-, with a gene frequency of 0.195, which is typical of the Cagliari province. A discriminant analysis on hematological variables revealed the classification: 210 normals, 72 beta-thalassemics, and 20 non-beta-thalassemics; the two types of thalassemia had very similar phenotypic frequencies. The relative frequencies obtained were: 192 nonthalassemics (82.4%), 19 non-beta-thalassemics (8.2%), and 22 beta-thalassemics (9.4%) in the random group. The main consequence of G-6-PD deficiency appears to be only a mild anemia with microcytosis. (23 refs.) - *A. C. Schenker.*

Universita di Roma
Roma, Italy

1853 DIOSI, P.; BABUSCEAC, LIVIA; & DAVID, CAMELIA. Distinctive cytopathic

properties of cytomegalovirus recovered from female genital tract. *American Journal of Clinical Pathology*, 59(2):192-195, 1973.

Significant differences are reported in the cytopathic effects produced in primary human embryonic skin muscle cell cultures by cytomegalovirus 3(CMV) isolates recovered from the female genital tract, compared with 5 isolates obtained from throat swabs. The cytopathic effect produced by oral CMV isolates progressed rapidly, involving the entire cell sheet in 7-9 days, in contrast to the genital CMV isolates which involved the sheet of fibroblasts only after 12-16 days. In the former, the infected cells became necrotic and disintegrated, leaving masses of refractile granules in the center of the foci surrounded by a thin border of rounded cells. In the latter case, there was a prolonged preservation of the integrity of affected cells, which adhered to one another and coalesced into dense compact plaques. The findings suggest that slow maturation in the nucleus of certain DNA viruses may cause modification of components of the cell surface responsible for the development of contacts with other cells. (23 refs.) - *A. C. Schenker.*

Medical Research Center
Timisoara, Rumania

1854 BRUPPACHER, RUDOLPH; & *DOMINGUE, GERALD. Experiences with a screening test for bacteriuria. *American Journal of Clinical Pathology*, 59(2):203-210.

Results of the Testuria dip test, a commercially produced test for bacteriuria, are compared with the calibrated loop technique on urine specimens from 252 patients in a urology outpatient clinic and 424 individuals undergoing routine examinations. The agreement between the two methods was apparent; sensitivity approached or exceeded the 90% level in individuals with bacteriuria, and the specificity was about the same. The predictive value was more than 95% for the negatives and more than 60% for the positives in the group with more than 100,000 bacteria/ml. When applied to a mass screening program, it was found that when the number of bacteria present was low, Testuria gave a greater number of false positives; approximately 10% of the population screened required follow-up studies. Where the incidence of bacteriuria is low, more conventional methods should be used in the follow-up. (10 refs.) - *A. C. Schenker.*

Tulane University School of Medicine
New Orleans, Louisiana 70112

1855 BENNET, JOHN E.; BONNER, HUGH; JENNINGS, ANNE E.; & LOPEZ, RAUL I. Chronic meningitis caused by Cladosporium trichoides. *American Journal of Clinical Pathology*, 59(3):398-407, 1973.

Cerebral infection with *Cladosporium trichoides* is described in a 17-year-old youth in whom bilateral carotid arteriogram revealed complete obstruction of the left internal carotid in the supraclinoid area. Other findings included a predominance of neutrophils in the cerebrospinal fluid and adhesions across the ventricles revealed by pneumoencephalography. Death was preceded by status epilepticus cardiorespiratory arrest. At postmortem, the ependymal surfaces in the brain were shaggy and irregular; glial adhesions were seen to bridge ventricular spaces; a small arachnoidal hemorrhage was found in the infratentorial portion; and irregular thinning of the spinal cord was seen. *Cladosporium trichoides* was isolated from pus at the base of the brain. The dermatomyocitic meningitis cannot be distinguished clinically from other chronic meningitides; demonstration of the etiologic agent by culture or histology is necessary. (49 refs.) - *A. C. Schenker.*

National Institutes of Health
Bethesda, Maryland

1856 PAPAGEORGIOU, P.S.; VERNANCE, S.; & GLADE, P.R. Hepatitis-associated antigen and cell-mediated immunity. *Lancet*, 1(7760):1118, 1972. (Letter)

A recent survey of 120 lepromatous and tuberculoid leprosy patients in a small residential grouping in Greece tends not to support Blumberg's suggestions that an impairment of cell-mediated immunity in the lepromatous patients is somehow related to an increased incidence of the hepatitis-associated antigen among these patients. These findings are in contrast to those resulting from studies in other geographical areas, such as the Philippines, and their significance should be further investigated. Additionally, institutionalization of leprosy patients appears not to be a factor of any special significance. Overall, the frequency of HAA in the 72 Greek lepromatous patients

studied was found by immunodiffusion and high voltage immunoelectrophoresis to be similar to the antigen's frequency in the Greek population at large: 1.4%, as compared to 1.8%. (6 refs.) - *N. Mize.*

Mount Sinai School of Medicine of
the City University of New York
New York, New York, 10029

1857 DEINHARDT, FRIEDRICH W. An epidemic of infective short-incubation hepatitis. *Lancet*, 1(7760):1118-1119, 1972. (Letter)

Continued use of the unfortunate term "epidemic hepatitis-associated antigen" (EHAA) can only further confuse scientific efforts to understand human hepatitis. Recent investigations by Thomas and others have proven conclusively that EHAA is a serum lipoprotein and is entirely unrelated to viral hepatitis or to any other specific liver disorder. Since the antigen has no actual immunological relationship to epidemics of short-incubation hepatitis, as has been previously suggested, the term should be dropped by serious investigators. (5 refs.) - *N. Mize.*

Rush-Presbyterian-St Luke's Medical
Center
Chicago, Illinois 60612

1858 CARVER, DAVID H.; & SETO, DEXTER S. Y. Current concepts concerning hepatitis viruses. *Pediatrics*, 51(1):115-119, 1973.

Recent work in connection with hepatitis viruses is reviewed. Blumberg's discovery of the Australia antigen led others to associate this antigen in the blood with hepatitis. Both the finding of Australia antigen in the feces of patients with hepatitis and the report of nonparenteral transmission of viral hepatitis add evidence for the spread of this agent by personal contact without ingestion. There is speculation by some investigators that the hepatitis B virus carries genetic information in the form of an RNA core. Studies have been done with both hepatitis A and hepatitis B in subhuman primates. Hepatitis B antigenemia, noted by all the investigators, was followed by the development of antibodies to the antigen. At present, many investigators are seeking an *in vitro* assay system for hepatitis A virus. Schweitzer and his colleagues have reported hepatitis and hepatitis-associated antigen in 56 mother-infant pairs. Standard immune serum globulin has not been shown to protect patients exposed to hepatitis B virus. With the known relationship between the presence of Australia antigen and hepatitis B virus, it is imperative that blood and blood products be screened for this antigen before being given to patients. (30 refs.) - *A. C. Schenker.*

Johns Hopkins University School
of Medicine
Baltimore, Maryland 21205

1859 MATSUDA, S.; TADA, K.; SHIRACHI, R.; & ISHIDA, N. Australia antigen in amniotic fluid. *Lancet*, 1(7760):1117, 1972. (Letter)

Of 59 parturient women in whom amniotic fluid and cord sera were examined by solid-phase radioimmunoassay, three had both Au-positive amniotic fluid and sera. While further research needs to be done, these findings may suggest a new mode of vertical transmission of the Au antigen. (1 ref.) - *N. Mize.*

Tohoku University School of Medicine
Sendai, Japan

1860 FERRIS, A. A.; PITT, D. B.; GUST, I. D.; & KALDOR, J. Australia antigen and Down's syndrome. *Lancet*, 1(7740):46, 1972. (Letter)

Microimmunodiffusion techniques were used to test for the presence of Australia antigen in sera from 182 inst Down's syndrome patients, from 167 other MR patients in the same inst, and from 110 non-inst Down's syndrome patients. The results emphatically confirm the earlier observations of Blumberg and others that the problem of Down's syndrome and serum hepatitis is clearly an inst one. None of the non-inst patients in this study showed any evidence of the Australia antigen. Among inst Down's syndrome patients, the Au-antigen carriage rate was 31.9%; among the other inst MR patients, the rate was only 5.4%. Additionally, the age distribution of these findings is compatible with the notion that the duration of the carrier state is significantly longer among Down's syndrome patients than among controls. (4 refs.) - *N. Mize.*

Monash University Medical School
Prahran, Victoria 3181, Australia

1861 **MELNICK, JOSEPH L.** A vaccine for viral hepatitis type B appears on the horizon. *New England Journal of Medicine*, 288(15):790-791, 1973.

A series of careful studies by Ward and Krugman on the natural history and prevention of viral hepatitis at the Willowbrook State School is reviewed and the promising results of a vaccine for viral hepatitis type B are commended. Follow-up studies of passive immunization have been extended for up to 1½ years on children receiving conventional immune serum globulin (ISG) or hepatitis B immune serum globulin (BISG) and then exposed to HB virus. Whereas conventional ISG proved ineffective in preventing HB infection, BISG produced evidence of protection in 7 of 10 children; however, 2 of the children became chronic HB antigen carriers. Highly promising results were obtained with human serum that contained HB Ag and was boiled for one minute. This inactivated vaccine induced HB antibody in 8 of 29 children, but it was fleeting in 6. It has recently been shown that subunits of HB Ag, consisting of small polypeptides, retain antigenicity; these may provide an ideal vaccine. (6 refs.) - *A. C. Schenker.*

1862 **KRUGMAN, SAUL; & GILES, JOAN P.** Viral hepatitis, type B (MS-2-strain): further observations on natural history and prevention. *New England Journal of Medicine*, 288(15):755-760, 1973.

The results of serial clinical and laboratory observations of groups of children who had a parenteral exposure to MS-2 serum are reported; this is an extension of a larger study on viral hepatitis type B. The Ss comprised 79 children: Group 1 included 25 susceptible children who received a parenteral inoculation of MS-2 serum (dose ranged between 0.1ml of a 1:10 dilution and 0.25ml); Group 2 included 15 susceptible children who received a 0.1ml of a 1:10 dilution of MS-2 serum parenterally and an inoculation of standard immune serum globulin 4 hr later (0.02ml/0.5kg in 5 Ss, and 0.06ml/0.5kg in 10 Ss); Group 3 included 10 susceptible Ss who received 0.1ml of a 1:10 dilution of MS-2 serum parenterally, followed by an inoculation of hepatitis B immune serum globulin (0.02ml/0.5kg) in 4 hrs; and Group 4 included 29 susceptible Ss of whom 10 received one inoculation of inactivated MS-2 serum, 4 received 2 inoculations at 4-month intervals, and 15 received 3 inoculations at 2-month intervals. All Group 4 Ss had a parenteral exposure to 0.1ml of a 1:10 dilution of MS-2 serum 4-8 months after the inoculations. The studies confirmed the previous observations that MS-2 heat-inactivated serum was not infectious and that it successfully prevented or modified hepatitis B virus infection. (16 refs.) - *A. C. Schenker.*

New York University Medical Center
New York, New York 10016

1863 **SCHWEITZER, IRVIN L.; WING, ADRIENNE; MCPEAK, CHRISTINE; & SPEARS, ROBERT L.** Hepatitis and hepatitis-associated antigen in 56 mother-infant pairs. *Journal of the American Medical Association*, 220(8):1092-1095, 1972.

Viral hepatitis and the hepatitis-associated antigen (HAA) were examined in 56 mother-infant pairs as part of a study to determine the frequency and mode of HAA transmission from mother to child and the duration of HAA antigenemia in the newborn children. All 56 mothers had typical acute viral hepatitis, as determined by the double diffusion technique, during pregnancy or within 6 months of delivery. Of the 26 mothers found HAA-positive during the acute illness, 10-all of whom had been infected near delivery—gave birth to HAA-positive infants. These 10 babies have been serially examined during a follow-up period of 3 to 23 months. All have remained consistently positive, but otherwise their physical and developmental status has been normal, with no clinical signs of hepatitis in evidence. In 3 cases, the antigen seemed to have crossed the placental barrier, while in at least one, neonatal contamination at birth seems to have been at fault. The long range effect of persistent antigenemia and protracted hepatitis in the children remains to be seen. (10 refs.) - *N. Mize.*

2826 S. Hope St.
Los Angeles, Calif. 90007

1864 **GRAND, M. GILBERT; WYLL, SHELBY A.; GEHLBACH, STEPHEN H.; LANDRIGAN, PHILIP J.; JUDELSOHN, RICHARD G.; ZENDEL, STEPHEN A.; & WITTE, JOHN J.** Clinical reactions following rubella vaccination. *Journal of the American Medical Association*, 220(12):1569-1572, 1972.

Joint, muscular, and neuritic symptoms were

surveyed in two groups of North Carolina and Louisiana children who received rubella vaccine of either the DE-5, DK-12, or Cendehill strain. The comparative incidence and characteristics of vaccine-associated reactions were determined by a prospective study. Parents were surveyed by mail during a 60-day post-vaccination period and those reporting specific reactions in their children were interviewed. Additionally, both prospective and retrospective control groups of comparable size were selected. Overall, the reaction rates for children receiving the DK-12 vaccine were significantly higher than those associated with the Cendehill or DE-5 varieties, a finding which did not show up in the earlier pre-licensure field trials. In contrast to the generally mild DE-5 and Cendehill reactions recorded, DK-120 vaccinees showed a later onset and longer duration of symptoms and a higher rate of arthritis and paresthesia. While factors other than vaccine strain may affect the associated reaction rates, the present evidence suggests that Cendehill and DE-5 rubella vaccines are safe for use in public immunization programs. (17 refs.) - *N. Mize*.

1600 Clifton Rd.
Atlanta, Georgia 30333

1865 **BEARE, A. S.; HALL, T. S.; & TYRRELL, D.A.J.** Protection of volunteers against challenge with A/Hong Kong/68 influenza virus by a new adamantane compound. *Lancet*, 1(7759):1039-1040, 1972.

Five separate double-blind trials showed that a new non-toxic adamantane compound was potentially effective in protecting against A/Hong Kong/68 influenza virus. Of 57 volunteers with low antibody titers to the virus, the 28 who had randomly received the drug showed fewer clinical symptoms, antibody rises, and virus excretions when challenged with the Type A influenza virus than did the 29 others treated with placebos. Even though the experimental compound did not prevent infection in all of the volunteers who received it, the results in this highly sensitive prophylactic trial tend to support the hope that the adamantane drug will be even more effective under actual field conditions. (16 refs.) - *N. Mize*.

Harvard Hospital
Salisbury, Wiltshire, England

1866 **JABBOUR, J. T.; DUENAS, D. A.; SEVER, J. L.; KREBS, HELEN M.; & HORTA-BARBOSA, L.** Epidemiology of subacute sclerosing panencephalitis (SSPE). *Journal of the American Medical Association*, 220(7):959-962, 1972.

Epidemiological data gathered by the Subacute Sclerosing Panencephalitis Registry have demonstrated a strong correlation between early onset of rubeola and the later development of SSPE. Of the 95 patients for whom the age of measles onset was known, 55% reported measles infection before 2 years of age. The registry obtained specific information on 219 SSPE patients seen by 104 medical centers across the country, from 1960 to 1970. Additional findings from the Registry's first complete report identify a significant concentration of patients in the southeastern U.S., an early age of SSPE onset (mean age, 7.2 yrs), a high ratio of male to female patients, and, contrary to previous suggestions, no clear rural residence association for patients at the time of diagnosis. Overall, the incidence of SSPE in the U.S. was approximately 1 per million childhood population over the 10-year period. (7 refs.) - *N. Mize*.

848 Adams Street
Memphis, Tennessee 38101

1867 **NELSON, ROBERT F.; DENNERY, JEAN M.; MONTPETIT, VITAL; & FURESZ, JOHN.** S.S.P.E. and pregnancy. *Lancet*, 1(1763):1289, 1972. (Letter)

A rare case of subacute sclerosing panencephalitis (SSPE), with onset in the third decade, is reported. Clinical symptoms first appeared during pregnancy in the 21-year-old woman. At the time, symptomatic personality changes were interpreted as being psychiatric in origin and the SSPE diagnosis was not made until post-partum. At 34 weeks gestation, the woman gave birth to a 5-lb infant who succumbed after 24 hrs to a fatal combination of RDS, severe anemia, and cephalo and subdural hematomas. Subsequent serum and cerebrospinal fluid measles antibody studies and cerebral biopsy in the mother, who had had clinical measles at age 2½ years, revealed typical SSPE findings. At necropsy, the infant's brain showed no evident histological effects from exposure to the disease throughout 8 mos of gestation. (4 refs.) - *N. Mize*.

University of Ottawa and Ottawa
General Hospital
Ottawa, Canada

1868 **MOSLEY, JAMES W.** Vertical transmission of type B hepatitis. *Journal of the American Medical Association*, 220(8):1128-1129, 1972. (Editorial)

Recent investigations of type B hepatitis have demonstrated that the epidemiology of this disease is multifaceted and much more complex than previously thought. While it is frequently associated with percutaneous medical procedures, this is not the only mode of transmission. The development of a sensitive test for hepatitis-associated antigen (HAA) has made it possible to demonstrate infection even in the absence of any apparent abnormalities. Transplacental infection has been conclusively demonstrated by the finding of HAA in cord blood. Paranatal and postnatal transmission are well established. Recent indications that transfer of type B hepatitis from mother to offspring, by whatever mechanism, is relatively common—10 babies of 26 HAA-positive mothers in one survey—make it essential that researchers further investigate the potential dangers to family and society associated with the expanding numbers of asymptomatic carriers. (3 refs.) - *N. Mize.*

John Wesley Hospital
Los Angeles, California

1869 Synthetic nucleoside fights viruses. *Journal of the American Medical Association*, 220(9):1187-1188, 1972.

A recently synthesized nucleoside, 1-B-D-ribofuranosyl-1,2, 4-triazole-3-carboxamide (RTC), may be the first of a series of new antiviral compounds. In preliminary animal tests and *in vitro*, the nucleoside, called Virazole by its developer, has proven active against several DNA and RNA viruses, especially those associated with influenza and other respiratory diseases. So far, RTC has shown no activity against poliovirus pseudorabies virus, or herpesvirus encephalitis, indicating that it probably doesn't cross the blood-brain barrier. The nucleoside has a broad antiviral spectrum and seems to work not by inducing interferon, but by preventing the formation of new virus particles through the blocking of an early step in the replication process. - *N. Mize.*

1870 **GILANI, SHAMSHAD H.** Congenital anomalies in lead poisoning. *Obstetrics and Gynecology*, 41(2):265-269, 1973.

The effects of lead on embryonic development were studied in 2-day-old chick embryos from White Leghorn stock. The fertilized eggs were incubated at 38.5 C and lead acetate was administered in varying doses (0.005-0.080 mg/egg) on day 2 of incubation. All embryos (720) were examined on day 8 of incubation for gross congenital malformations under the dissecting stereomicroscope. The results revealed a clear dose-dependent effect; survival was 87% when the dose inoculated was 0.005mg/egg and decreased to 9% with a dose of 0.080mg/egg. Principal teratogenic effects were: retardation of body size, micromelia, shortened neck, ruptured brain, shortened beak, twisted neck and limbs, and everted viscera. The high incidence of neck abnormalities suggests that lead may interfere with some specific proteins at the critical stage in which cervical spines develop. The retarded body growth indicates that lead has a general inhibitory action on metabolism. (14 refs.) - *A. C. Schenker.*

New Jersey Medical School
Newark, New Jersey 07103

1871 **DI MUSTO, JUAN C.; BOHJALIAN, OSHIN; & MILLAR, MARY.** Mycoplasma hominis type I infection and pregnancy. *Obstetrics and Gynecology*, 41(1):33-37, 1973.

The effects of the presence of *Mycoplasma hominis* type I in the vagina of pregnant women on the outcome of these pregnancies were studied in 100 such patients. Positive cultures for Mycoplasma were selected using the 3 colony criteria of Madoff: "fried egg" colonies that penetrated the agar; development of large bodies of various sizes; and softness of the colonies. Type identification was made by the growth inhibition method of Chanock. The incidence of infection of this type among pregnant women examined was 23%; total mycoplasma (large colonies) infection revealed an incidence of 33%. Only 27 placental cultures and 26 cultures from the infants' axilla were obtained. Of the 3 cases with positive cultures from the placenta and axilla, 1 was a 1-pound, 2-ounce premature who lived a few hours; the second, a 5-pound, 7-ounce normal baby who succumbed to "crib death" at 20 days; and the third was a normal infant who fared well. A cause-effect relationship cannot be postulated from these results. (12 refs.) - *A. C. Schenker.*

Crittenton Hospital
Detroit, Michigan 48206

1872 **JORDAN, M. COLIN; ROUSSEAU, WYATT E.; NOBLE, GARY R.; STEWART, JOHN A.; & *CHIN, TOM D. Y.** Association of cervical cytomegaloviruses with venereal disease. *New England Journal of Medicine*, 288(18):932-934, 1973.

The incidence of cytomegaloviruses (CMV) in nonpregnant women was investigated and factors associated with cervical shedding of CMV in these Ss were sought. Participants were divided into: Group I, comprising 76 nonpregnant women undergoing gynecologic examination (premarital or required), and Group 2 (120 Ss), undergoing examination for suspected venereal disease. Cervical swab specimens were collected from all Ss and serum samples from 150 women. CMV was not isolated from any of the Group 1 Ss, and 16 of the Group 2 Ss (13.3%) were shedding CMV ($p<0.001$). Among all the Ss, CMV was isolated from 10 of 70 (14.3%) with documented past or active gonococcal infection as compared with 6 of 126 (4.8%) with no such infections ($p<0.02$). CMV was recovered only from women in Group 2, among whom a significantly greater frequency of venereal infection with N. gonorrhoeae and HVH-2 was found, although the actual presence of gonococci in the cervical secretions at the time of sampling for viral studies did not correlate significantly with recovery of CMV. If sexual transmission of CMV does occur, it remains to be determined whether genital acquisition can cause dissemination of CMV mononucleosis or other forms of systemic illness. (19 refs.) - *A. C. Schenker.*

Center for Disease Control
Kansas City, Kansas 66103

1873 **INGALLS, THEODORE H.; HORNE, HERBERT W., JR.; MARSH, EDWARD B.; & PHILBROOK, F. RANDOLF.** Efficacy of rubella vaccines. *New England Journal of Medicine*, 288(16):855, 1973. (Letter)

In connection with reports regarding the limitations of rubella vaccines, a third vaccine, RA27/3, does not seem to share such theoretical limitations. RA27/3 is effective when administered either subcutaneously or intranasally, giving rise to antibodies in the immunoglobulins of the nasal mucosa by either route. This vaccine is also effective in boosting immunity in those vaccinated several years earlier with other vaccines. It is urged that RA27/3 be licensed and made available on a basis of equality with HPV-77 and Cendehill vaccines for use in daily patient care. - *A. C. Schenker.*

1874 **XANTHOU, M.; NICOLOPOULOS, D.; GIZAS, A.; & MATSANIOTIS, N.** The response of leukocytes in the peripheral blood during and following exchange transfusion in the newborn. *Pediatrics*, 51(3):570-574, 1973.

The response of the white blood cells during exchange transfusion in the newborn and for 7-9 days thereafter is reported. Twenty-seven such transfusions were done on 20 jaundiced but otherwise healthy babies, of whom 12 were full term (birthweight 2,600-3,700gm) and 8 were premature (1,750-2,400gm). There was a marked decrease in the absolute values of polymorphonuclear neutrophils during the procedure, followed by a marked increase soon after and reaching a peak within a week. Although these values and those of eosinophils were significantly higher following the exchange transfusion than those in normal babies, the lymphocytes were not increased and the monocytes were decreased. The most likely mechanism responsible for these changes seems to be the displacement of neutrophils from the marginal layer of vessels and of all leukocyte types from extravascular pools. (17 refs.) - *A. C. Schenker.*

Athens University, St. Sophie's
Children's Hospital
Athens, 608, Greece

1875 **CRAMBLETT, HENRY G.; HAYNES, RALPH E.; AZIMI, PARVIN H.; HILTY, MILO D.; & WILDER, MICHAEL H.** Nosocomial infection with echovirus type II in handicapped and premature infants. *Pediatrics*, 51(4):603-607, 1973.

An outbreak of echovirus type 2 infection among premature and/or handicapped infants in an intensive care unit is described; details of 4 cases are given. The virus was recovered from multiple specimens of the 4 infants and from a practical nurse and medical student who worked on the unit, but not from other infants on the unit who were not ill. The illness was acute and the clinical findings suggested bacterial sepsis and/or bacterial meningitis. The fact that 3 of the patients became

ill within 24 hours of one another suggests that they were exposed and infected at nearly the same time; personnel transmission is suggested. The outbreak was halted by removing the ill infants to the infectious disease area and by closing the involved unit to new admissions for 7 days. The occurrence of nosocomial infections due to viruses among hospitalized patients is particularly stressed. (17 refs.) - *A. C. Schenker.*

Children's Hospital Research
Foundation, Inc.,
Columbus, Ohio 43205

1876 **CHISOLM, J. JULIAN, JR.** Screening for lead poisoning in children. *Pediatrics*, 51(2):280-283, 1973.

A simple and rapid method of screening for lead toxicity is discussed; it is the protoporphyrin (PROTO) assay which can be carried out in capillary blood samples. Micro procedures for this assay are adaptable to suitably equipped filter fluorometers. The concentration of lead in peripheral blood provides the most useful index of current and recent absorption of lead and is an essential measurement in suspected cases of lead poisoning. Since the relationship between PROTO and lead in blood is curvilinear and PROTO increases exponentially as blood lead concentration rises arithmetically above the 30-50 microgram Pb threshold, the inherent analytical variation in PROTO assay of up to 10% is minor in comparison with the inherent variation of 5% to 10% in blood lead analyses. The doubtful zone by the PROTO test is apparently associated with blood lead concentrations in the 30-50 microgram Pb range. The higher levels which are associated with overt plumbism are clearly identified by the PROTO test. (16 refs.) - *A. C. Schenker.*

Baltimore City Hospitals
Baltimore, Maryland 21224

1877 **WEIBEL, ROBERT E.; BUYNAK, EUGENE B.; STOKES, JOSEPH, JR.; & *HILLEMAN, MAURICE R.** Persistence of immunity following monovalent and combined live measles, mumps, and rubella virus vaccines. *Pediatrics*, 51(3):467-475, 1973.

Follow-up studies to measure persistence of antibody and/or protection following several monovalent or combined vaccines are presented. Jeryl Lynn mumps virus vaccine, now past its sixth year, has demonstrated persistence of antibody in closed as well as open populations and the persistence of protection against the natural disease. The Enders' original and the further attenuated measles virus vaccines all show persistence of antibody through 4 years in the present study. Antibody has been shown to persist for at least 3½ years after HPV-77 duck rubella vaccine. Combination of measles, mumps, and rubella vaccines does not decrease the height of the antibody responses of the individual vaccines, and no alteration in the pattern of persistence is found. (21 refs.) - *A. C. Schenker.*

Virus and Cell Biology Research
Merck Institute for Therapeutic
Research
West Point, Pennsylvania 19486

1878 **HEINEMAN, HERBERT S.; & LEE, JAMES H.** Bacteriuria in pregnancy: a heterogeneous entity. *Obstetrics and Gynecology*, 41(1):22-26, 1973.

The relationship of complications arising from bacteriuria in pregnancy to the origin of infection in either bladder or kidneys was investigated. Of a total of 700 women who were screened for asymptomatic bacteriuria, 68 (9.7%) were positive and of these, 53 returned for bladder washout to determine the site of infection. Renal bacteriuria, diagnosed when urine entering the bladder appeared more heavily infected than the bladder contents after washout, was found in 13 patients; 19 patients had cystic bacteriuria, as indicated by the fact that only sterile urine entered the bladder; and for 7 patients the site of infection was undetermined. In 14 patients, infection had disappeared spontaneously in 2-19 days after screening. Since women with asymptomatic bacteriuria are more susceptible to pyelonephritis, it is important to determine the site of infection by reliable techniques. Criteria for verifying the reliability of screening cultures recommended for this purpose are: aseptic catheterization and isolation of significant numbers of bacteria in pure culture. (14 refs.) - *A. C. Schenker.*

Hahnemann Medical College
Philadelphia, Pennsylvania 19102

1879 **ORZALESI, MARCELLO; GLORIA, FULVIA; LUCARELLI, PAOLA; & BOTTINI, EGIDIO.** ABO system incompatibility: relationship between direct Coombs

test positivity and neonatal jaundice. *Pediatrics*, 51(2):288-289, 1973.

Since newborn infants with ABO incompatibility with their mothers present a potentially higher risk of severe hyperbilirubinemia, particularly in the presence of a positive direct Coombs test, a series of such infants was studied to discover whether they were threatened with neonatal jaundice before it actually developed visibly. A direct Coombs test was performed on cord blood in all infants who were incompatible with their mothers in the ABO or in the Rh system or both. The presence of jaundice was significantly associated with Coombs test positivity; infants with ABO incompatibility and a positive Coombs test carried a risk of neonatal jaundice which was about 4 times higher than infants with a negative Coombs test. Infants with ABO incompatibility and a positive Coombs test developed neonatal jaundice in approximately 50% of the cases and a serum bilirubin level higher than 10mg/100ml in 25%. A direct Coombs test on cord blood should be included in any program aimed at the prevention of severe hyperbilirubinemia. (5 refs.) - *A. C. Schenker.*

Citta Universitaria
00185 Rome, Italy

1880 BALFOUR, HENRY H., JR.; SEIFERT, GREGORY L.; SEIFERT, MILTON H., JR.; QUIE, PAUL G.; EDELMAN, CHARLENE K.; BAUER, HENRY; & SIEM, ROBERT A. Meningoencephalitis with California encephalitis virus, echovirus II, and mumps. *Pediatrics*, 51(4):680-684, 1973.

Laboratory evidence of simultaneous infections with 3 antigenically distinct viral agents in the presence of acute nervous system disease is reported; these were the California encephalitis virus (CEV), echovirus type II, and mumps. The patient was a 6-year-old girl who was hospitalized with fever and seizures. Echovirus type II was isolated from a stool specimen on the sixth hospital day; the child had a fourfold rise in echovirus II neutralization (Nt) antibody. Infection with the La Crosse strain of CEV was diagnosed by a greater than fourfold rise in La Crosse III, complement fixation (CF), and Nt antibody titers and by acquisition of precipitin antibody in the convalescent serum specimen. The patient also showed a fourfold rise in her mumps viral (V) CF antibody titer. The patient had received live, attenuated mumps vaccine 14 months previously; the boost in mumps CF antibodies could reflect an asymptomatic infection with wild mumps virus resulting in anamnestic immunologic response. It is also possible that infection with either CEV or echovirus II may have been responsible for the heterotypic boost in mumps antibodies. (15 refs.) - *A. C. Schenker.*

University of Minnesota Health
Science Center
Minneapolis, Minnesota 55455

1881 PLUNKETT, GUY D. Neonatal complications. *Obstetrics and Gynecology*, 41(3):476-477, 1973. (Letter)

Four cases of neonatal complications attributed to intraamniotic injection of methylene blue dye for the diagnosis of premature rupture of the membranes are reported. The 4 neonates, delivered of mothers who received such an injection of 3.5ml 1% dye from 24 hours to 5 weeks before delivery, developed hemolytic anemia and hyperbilirubinemia; 2 of these infants developed sepsis and 1 died of gram-negative septicemia. It is recommended that instead of using a dose of 30-50mg of methylene blue for this procedure, 5ml of a dilute solution (1.0ml of a 1% methylene blue in 30ml saline) which corresponds to 1.6ml is satisfactory for confirming the presence of ruptured membranes. (1 ref.) - *A. C. Schenker.*

Brooke Army Medical Center
Fort Sam Houston, Texas 78234

1882 LEPPERT, PHYLLIS C. Toxemia. *Obstetrics and Gynecology*, 41(3):475-476, 1973. (Letter)

Since there are no clear cut criteria for diagnosing toxemia of pregnancy, the term toxemia ought to be discarded as meaningless and obscure. If proper records are kept of the triad hypertension, edema, and/or proteinuria, patients can be treated for these problems as they are currently treated. As other data become available, a specific diagnosis can then be made. Only when glomerular endotheliosis on renal biopsy is definite should the diagnosis of pregnancy-specific acute hypertension be applied. Only by using precise terms in this connection can the illness be investigated from the viewpoint of the accumulation of data related to

specific conditions in pregnancy. (6 refs.) - *A. C. Schenker.*

Duke University Medical Center
Durham, North Carolina 27706

1883 **LOGOTHETIS, JOHN; LOEWENSON, RUTH B.; AUGOUSTAKI, OLGA; ECONOMIDOU, JOANNA; & CONSTANTOULAKIS, MATHIOS.** Body growth in Cooley's anemia (homozygous beta-thalassemia) with a correlative study as to other aspects of the illness in 138 cases. *Pediatrics*, 50(1):92-99, 1972.

A cross-sectional study of 77 male and 61 female verified cases of Cooley's anemia (homozygous beta-thalassemia) aged 2 to 28 years living in the Athens area of Greece revealed a retardation in height and weight (except for children under age 4) but not in head size. By the age of 9 to 10 years, the average height of the thalassemic children was 1 standard deviation below the mean height for normals. The degree of anemia manifested only slight correlation with the extent of height and weight retardation, but the increase in some of the systemic abnormalities generally reflecting the severity of the thalassemic disorder showed a general tendency to parallel these retardations, especially that of height. The trend found for higher IQ scores to be associated with children with better physical growth, who were also those with a less severe illness, was probably related to the superior educational opportunities and social stimulation afforded to them. (19 refs.) - *B. J. Grylack.*

University of Minnesota Medical
School
Minneapolis, Minnesota

1884 **BALFOUR, HENRY H., JR.; MAY, DONALD B.; ROTTE, THOMAS C.; PHELPS, W. RICHARD; & *SCHIFF, GILBERT M.** A study of erythema infectiosum: recovery of rubella virus and echovirus-12. *Pediatrics*, 50(2):285-290, 1972.

In a virologic investigation of specimens from 102 children with erythema infectiosum (fifth disease), 10 patients (9.8%) had a laboratory diagnosis of associated rubella infection, and 4 children (3.8%) showed evidence of echovirus-12 infection. Although the incidence of lymphadenopathy was greatest in the rubella-associated group, analysis of the clinical data did not provide distinctions between the individual cases associated with rubella or echovirus-12 and the 88 patients with no laboratory evidence for viral infection. The data suggested that 14 (14%) of the 102 erythema infectiosum patients had dual infections or that perhaps they were infected with a strain of rubella virus that produced an illness resembling erythema infectiosum. In preliminary testing of rubella virus isolates in human volunteers, a viral challenge pool derived from the pharyngeal swab isolate of 1 study patient was found to produce an exanthem resembling erythema infectiosum in some individuals. (11 refs.) - *B. J. Grylack.*

Department of Medicine, K-4
Cincinnati General Hospital
Cincinnati, Ohio 45229

1885 **AVRUSKIN, THEODORE W.; BRAVERMAN, LEWIS E.; & CRIGLER, JOHN F., JR.** Thyroxine-binding globulin deficiency and associated neurological deficit. *Pediatrics*, 50(4):638-645, 1972.

A report of 4 MR males, all from a single family, with hereditary thyroxine-binding globulin (TBG) deficiency is the first in which associated mental and neurological defects have been present. The mode of inheritance in this family was X-chromosome-linked. The propositi showed absence of thyroxine (T_4) binding to serum TBG and significant abnormalities in neurological function. No other specific causes of neurological impairment could be demonstrated, although the remote possibility that the family had an increased propensity for MR of unknown etiology, unrelated to TBG deficiency, could not be excluded. The propositi were clinically and chemically euthyroid. The evidence suggests that the inheritance patterns of MR and the X-linked chromosome disorders are related, with the gene loci for these 2 characteristics both on the long arm of the X chromosome and possibly in proximity. (26 refs.) - *B. J. Grylack.*

Brookdale Hospital Medical Center
Division of Pediatric Endocrinology
and Metabolism
Brooklyn, New York 11212

1886 **CHERRY, JAMES D.; FEIGIN, RALPH D.; LOBES, LOUIS A., JR.; & SHACKELFORD, PENELOPE G.** Atypical measles in children previously immunized with

attenuated measles virus vaccines. *Pediatrics*, 50(5):712-717, 1972.

In a group of 12 children with clinical illnesses suggesting the "atypical measles" syndrome during a measles epidemic, aberrant exanthems occurred in the 6 children who received only live vaccine. The symptoms of the groups receiving inactivated killed or attenuated live vaccines were very similar, but illness was more severe in recipients of the killed vaccine. The geometric mean hemagglutination-inhibiting antibody titer of the acute serums in the recipients of live vaccine was greater than that of the other children, while the converse was true of the convalescent serum titers. The possibility that the live vaccine had been inactivated inadvertently should not be ruled out, in view of the rarity and decreased severity of the atypical measles syndrome following live measles vaccine. (21 refs.) - *B. J. Grylack*.

Cardinal Glennon Memorial Hospital
for Children
St. Louis, Missouri 63104

1887 **ST. GEME, JOSEPH W.; & NOREN, GEORGE R.** Mechanisms of fetal immune response. *New England Journal of Medicine*, 287(10):518, 1972. (Letter)

Observations by Cohen concerning split tolerance do not rule out the hypothesis that abbreviated replication of mumps virus in the immature fetus permits the active induction of only T-cell mediated immunity. - *V. J. Goldberg*.

Harbor General Hospital
Torrence, California

1888 **WOODROW, J. C.** Fetal/maternal incompatibility. *Lancet*, 2(7786):1095-1096, 1972. (Letter.)

The article of Nov. 4, 1972 (p. 957) may be misleading in regard to the degree of protection against Rh sensitization afforded by ABO incompatibility between mother and fetus. The possibility that the majority of ABO incompatible matings can produce ABO compatible infants and that Rh sensitization occurs more frequently among ABO compatible pregnancies was not considered in the estimate of the protective value of ABO incompatibility. Our data show that the incidence of anti-D 6 mo after the delivery of a first Rh positive, ABO incompatible child was 0.82% vs 8.2% following the delivery of an Rh positive, ABO compatible child. Another finding is that when antibody develops during a second pregnancy when the first pregnancy was ABO incompatible, the second pregnancy is usually ABO compatible. (5 refs.) - *V. J. Goldberg*.

University of Liverpool (Medicine)
Liverpool L69 3BX England

1889 **BARR, R. D.; & CARTY, M. J.** Fetal/maternal incompatibility. *Lancet*, 2(7786):1096, 1972. (Letter.)

We disagree with the statement in the article of Nov. 4, 1972 (p. 957) that the blood found in the abdominal cavity following the rupture of a tubal pregnancy should not be used for autotransfusion in order to avoid the risk of rhesus isoimmunization. The advantages of autotransfusion clearly outweigh the risk as there is no documentation of rhesus immunization following the rupture of an ectopic pregnancy. Autotransfusion is a lifesaving technique, especially where sophisticated medical facilities do not exist. (5 refs.) - *V. J. Goldberg*.

University of Aberdeen (Medicine)
Foresterhill
Aberdeen AB9 2ZD, Scotland

1890 **TABB, P. A.; INGLIS, J.; SAVAGE, D.C.L.; & WALKER, C.H.M.** Controlled trial of phototherapy of limited duration in the treatment of physiological hyperbilirubinaemia in low-birth-weight infants. *Lancet*, 2(7789):1121-1212, 1972.

The prophylactic value of 12 hr or 24 hr of phototherapy in physiological jaundice was investigated in 78 low birthweight neonates (less than 2500g) who had serum bilirubin levels of 10mg/100ml (indirect) or more. Twenty-six of 78 received no phototherapy, but 11 had subsequent serum bilirubin levels greater than 13mg/100ml and required phototherapy. Twenty-nine of 78 received 12 hr of phototreatment (100-200 footcandles of light), and 7 of these required additional phototherapy; 23 of 78 received 24 hr of phototherapy and 4 required further treatment. The need for additional treatment occurred more often among preterm neonates whose serum bilirubin levels rose quickly and exceeded 10mg/100ml within 72 hrs of birth. Bilirubin levels should be monitored for 2-3 days after phototherapy to detect failure or rebound. The

use of 12 hr of phototherapy has eliminated the need for exchange transfusions (except in rhesus disease) and the administration of phenobarbitone to infants who are at risk of physiological jaundice. (21 refs.) - *V. J. Goldberg.*

Royal Infirmary and Maryfield Hospital
Dundee, Scotland

1891 **O'RIORDAN, J. P.** Fetal/maternal incompatibility. *Lancet*, 2(7786):1095, 1972. (Letter)

In addition to the routine dosage of anti-D IgG given to cesarean section patients with Rh incompatibility, the administration of this compound intraperitoneally at the time of abdominal surgery may give additional protection against the problems arising from the transfer of fetal cells across the peritoneum. (1 ref.) - *V. J. Goldberg.*

Blood Transfusion Service Board
Dublin 2, Ireland

1892 **AMSTEY, MARVIN S.; & KOBOS, KATHERINE.** An experimental model for disseminated neonatal herpesvirus infection. *Obstetrics and Gynecology*, 41(4): 634, 1973. (Abstract)

Experiments designed to reproduce in mice a situation which represents the pathogenesis of human neonatal herpesvirus infection are described. Pregnant and nonpregnant adult female mice were inoculated with type 2 herpesvirus by intravaginal tampons soaked with a virus concentration of 3.5 $\log_{10}$ TCD_{50} 0.2 ml. The susceptibility difference between pregnant and nonpregnant animals was evaluated by noting differences in death rate due to virus and virus isolation from various organ tissues. Newborn mice from infected mothers were observed for 3 weeks after delivery, and groups of neonates were sacrificed daily to follow the onset and course of virus infection. Approximately 60% of these newborn mice died of this infection. Of those newborns sacrificed, herpesvirus was isolated from the liver, adrenals, and/or brains of 40-50%. This system accurately reproduced the human situation in cases of congenital infection. - *A. C. Schenker.*

University of Rochester
School of Medicine and Dentistry
Rochester, New York

1893 **ROBBINS, FREDERICK C.** Low-level immunity to rubella. *New England Journal of Medicine*, 287(12:615, 1972. (letter).

It is questionable whether the patient discussed by Northrop et al. had prior immunity to rubella, as an HI-antibody titer of 20 on the second day of clinical rubella is not an unusual finding in primary rubella infection, and one rarely sees full-blown rubella in a person with prior immunity. (3 refs.) - *V. J. Goldberg.*

Case Western Reserve University
School of Medicine
Cleveland, Ohio

1894 **SMITH, ARNOLD L.** Therapy of influenzal meningitis considered. *New England Journal of Medicine*, 287(13): 664-665, 1972. (Editorial)

The efficacy of ampicillin vs chloramphenicol therapy in *Haemophilus influenzae* meningitis depends on the concentration of antibiotic in the CSF. Parenterally administered penicillin G does not cross the blood brain barrier except in the presence of inflammation, while chloramphenicol passes into the CSF without difficulty. Intrathecal administration of the antibiotic (as is done with streptomycin) can overcome this problem. A major problem is to maintain high CSF drug levels during the recovery phase when inflammation has subsided, but bacteria are still present. Since the incidence of MR sequelae of *H. influenzae* infection has remained at 40%, despite decreases in mortality, efforts should be made to prevent the disease. (7 refs.) - *V. J. Goldberg.*

1895 **ZIMMERMAN, HYMAN J.** VA study with hepatitis B immune globulin. *New England Journal of Medicine*, 287(13):670, 1972. (Letter).

The Veterans Administration has initiated a multicenter cooperative study on the usefulness of hepatitis B immune globulin in the prevention of hepatitis in accidental parenteral exposure to hepatitis B antigen. This study should not be confused with a similar project conducted by the National Heart and Lung Institute. - *V. J. Goldberg.*

Veterans Administration Hospital
Washington, D. C.

1896 **NORTHROP, ROBERT L.; GARDNER, WILLIAM M.; & GETTMANN, WILLIAM F.** Low-level immunity to rubella. *New England Journal of Medicine*, 287(12):615, 1972. (Letter)

Vaheri et al. (N Engl J Med 286:1071-1074,1972) may have overstated the protective value of low-level of rubella virus HI antibody. A 7-wk pregnant woman had rubella virus HI antibody titer of 20 on the second day of clinical rubella and HI titer of 320 2 wks later. The virus was isolated from the aborted fetus, which indicates that fetal infection can follow reinfection with 'wild' rubella virus. The case raises the question whether vaccine-induced antibody titers will protect prepubertal girls from subsequent rubella infection. (2 refs.) - *V. J. Goldberg.*

Rush-Presbyterian-St. Luke's
Medical Center
Chicago, Ill.

1897 **JARNEROT, GUNNAR; & LANTORP, KURT.** Antibodies to EB virus in cases of Crohn's disease. *New England Journal of Medicine*, 186(22):1215-1216, 1972. (Letter)

The antibody titers to Epstein-Barr virus antigen among patients with Crohn's disease (25), ulcerative colitis (12), hemorrhagic proctitis (5), and blood donors (17) were similar. This is evidence against an etiologic role of Epstein-Barr virus in Crohn's disease. (2 refs) - *V. J. Goldberg.*

Linkoping University Medical
School
Linkoping, Sweden

1898 **JOHNSON, RICHARD T.** Effects of viral infection on the developing nervous system. Seminars in medicine of the Beth Israel Hospital, Boston. *New England Journal of Medicine*, 287(12):599-603, 1972.

A number of viral infections in laboratory animals induce sequelae resembling primary defects in neuroembryogenesis. Infection of chick embryo with influenza A virus resulted in failure of neural tube development, but no viral antigen was found in the neural ectoderm or in the surrounding mesenchyme. The nature of the malformation following inoculation of fetal lambs with blue tongue virus depended on fetal age. Infection of the germinal cells of the telencephalon, but not of the vascular endothelium, was found. Other viruses affecting mitotic, migrating, or differentiating cells are rat viruses, feline panleukopenia, minute virus of mouse, lymphocytic choriomeningitis (rat), and hog cholera. Viruses affecting differentiated cells, but with the defect resembling agenesis, are mumps, parainfluenza II, influenza (hamster), reovirus type I, and Ross River (mouse). The possibility that human malformations may also be caused by viruses should be investigated. These studies also pertain to the use of live-virus vaccines on pregnant women. (20 refs.) - *V. J. Goldberg.*

Johns Hopkins University
School of Medicine
Baltimore, Md 21205

1899 **GLASGOW, ALLEN M.** Lean Reye syndrome: reply by Dr. Glasgow. *American Journal of Diseases of Children*, 125(6):901, 1973. (Letter)

In answer to comments submitted by Glick in connection with the article on Reye's syndrome in the absence of severe fatty infiltration, some of the points made are answered: to the implication that the prothrombin activity and venous ammonia level are not out of the range of normal values, it is pointed out that of 27 patients with acute encephalopathy of another etiology and 20 children without encephalopathy or liver disease, only one had an ammonia level above 0.1 milliM/ml, whereas case 1 had a higher ammonia level on 3 occasions; in the 27 patients with encephalopathy, 5 had a prothrombin activity of less than 60%. The low prothrombin activity and elevated ammonia level are good evidence for Reye's syndrome. Other positive features were some of the microscopic findings in the biopsy specimen of the liver. All of the findings in Dr. Glick's case are also nonspecific when taken singly. It would be important to discover how quickly the fatty infiltration of the liver occurs in the Reye syndrome. (3 refs.) - *A. C. Schenker.*

University of Colorado Medical
Center
Denver, Colorado 80220

1900 **GLICK, THOMAS H.** Lean Reye syndrome. *American Journal of Diseases of Children*, 125(6):900-901, 1973. (Letter)

Comments are submitted regarding the report by

Glasgow on the occurrence of Reye syndrome in the absence of severe fatty infiltration of the liver. Case 1 is considered a dubious clinical example of this syndrome, since some of the chemical determinants of the diagnosis are not sufficiently significant. Case 2 does have the essential features of the Reye syndrome, save for severe fatty change. Another such case is described briefly without evidence of fatty change in the liver biopsy. More detailed studies of such patients are needed before a pathophysiologically defined Reye syndrome can be definitely accepted. In addition to serial biochemical measurements, correlated with ultrastructural observations, complete autopsy examination should be done. (3 refs.) - *A. C. Schenker.*

Massachusetts General Hospital
Boston, Massachusetts 02114

1901 **FELDMAN, ROBERT G.; HADDOW, JAMES; KOPITO, LOUIS; & SCHWACHMAN, HARRY.** Altered peripheral nerve conduction velocity: chronic lead intoxication in children. *American Journal of Diseases of Children*, 125(1):39-41, 1973.

Minimal peripheral neurotoxic effects of increased lead burden were studied in relation to motor nerve conduction in children. The control Ss were 22 children aged 19 mos through 10 years, selected from nonrisk residential areas; motor nerve conduction velocities ranged from 44 to 68 meters/sec (mean = 52.78). Conduction velocity was measured in 24 children known to have had one or more of: blood lead levels greater than 40microgm/100gm of blood; more than 600mg/24hr excreted in urine following edetic acid provocation; radiographic evidence of lead-lines or radiopaque flecks in the gastrointestinal tract. The mean motor conduction velocity of the lead group was 42.33 meters/sec; the difference between the groups was significant ($p<.001$). Various stages of demyelination are found with chronic lead intoxication; conduction velocity will be affected only when a critical alteration in myelin exists. Slowing of nerve conduction velocity requires sufficient time for the changes in peripheral nerve fibers to take place. A relationship possibly exists between neuropathy and chronic exposure to lead. (21 refs.) - *A. C. Schenker.*

80 E. Concord St.
Boston, Massachusetts 02118

1902 **KAMMHOLZ, LARRY P.; THATCHER, L. GILBERT; BLODGETT, FREDERIC M.; & GOOD, THOMAS A.** Rapid protoporphyrin quantitation for detection of lead poisoning. *Pediatrics*, 50(4):625-631, 1972.

A screening method for lead intoxication in children by estimation of free erythrocyte protoporphyrin (FEP) in capillary blood is described. A sample of 0.1cc capillary blood is added to ethyl acetate-glacial acetic acid mixture and stirred to break up the red cells. After standing, the supernatant is decanted and the ethyl acetate-glacial acetic mixture again added to the red cell debris. The supernatants are combined and treated with hydrochloric acid, and 3 extractions are combined and read in a fluorimeter. The method measures coproporphyrin as well as protoporphyrin, but the former is present in low proportions. Distinct correlations were found between blood and FEP fluorescence, and significant correlation with the FEP fluorescence levels was seen with bone x-rays for deposits and abdominal x-rays for ingested lead material. The test for FEP, in addition to being useful as a screening test for lead intoxication, may also be useful for rapid general assessment of the potential severity of the intoxication. (13 refs.) - *A. C. Schenker.*

Medical College of Wisconsin
Milwaukee Children's Hospital
Milwaukee, Wisconsin

1903 **YEUNG, C. Y.** Serum 5'-nucleotidase in neonatal hepatitis and biliary atresia: preliminary observations. *Pediatrics*, 50(5):812-814, 1972.

Serum 5'-nucleotidase (5'N) was evaluated in 36 Chinese infants within the first 4 weeks of birth who had either biliary atresia or neonatal hepatitis and in 24 healthy infants; the value of this enzyme as a diagnostic measure was investigated. The results revealed that infants with extrahepatic biliary atresia had much higher levels of 5'-N ranging from 35 IU/liter-99 IU/liter; the highest level in neonatal hepatitis was only 23 IU/liter; normal controls had a mean value of 4.0±2.4. There were no differences in alkaline phosphatases and in transaminases between the 2 diseased groups. The 5'N determination is thus of diagnostic value in differentiating biliary atresia from neonatal hepatitis. (15 refs.) - *A. C. Schenker.*

McMaster University
Hamilton, Ontario, Canada

1904 **SMITH, EDWARD W. P., JR.; & *HAYNES, RALPH E.** Changing incidence of Hemophilus influenzae meningitis. *Pediatrics*, 50(5):723-727, 1972.

The increasing incidence of *Haemophilus influenzae (H. influenzae)* meningitis is reviewed with respect to a possible relationship to the number of hospital admissions. A predictable relationship of this nature could not be demonstrated by a number of studies of different periods: 1942-1950, 1951-1959, and 1960-1968. In most reported studies of *H. influenzae* meningitis 95% of all cases occur in children under 5 years of age, these children constituting the population at risk. Recent reports suggest a greater susceptibility of neonates to this infection because of low titers of bactericidal antibodies in maternal sera. Incidence stated in terms of population at risk appears to be a reliable method of comparing different geographic areas. (12 refs.) - *A. C. Schenker.*

The Children's Hospital
Columbus, Ohio 43205

1905 **RIE, HERBERT E.; HILTY, MILO D.; & CRAMBLETT, HENRY G.** Intelligence and coordination following California encephalitis. *American Journal of Diseases of Children*, 125(6):824-827, 1973.

The effects of California encephalitis on psychological and visual-motor coordination functioning were assessed in 29 children in a follow-up study 2 years following the illness. No differences emerged in comparisons of these children with a control group. The comparison included: ratings of degree of organicity, tested by subscale scores of the Wechsler Intelligence Scale for Children (WISC) and the Bender test; full scale IQs (WISC); and Koppitz scores of the Bender test protocols. Comparisons of preillness and postillness functioning of 9 of the children suggest that some effects may be noted in a few children who were severely ill and relatively recently ill. The results also suggest that intellectual functioning and/or visual motor coordination may be found more often if focal neurological signs appeared during illness. (4 refs.) - *A. C. Schenker.*

Children's Hospital
Columbus, Ohio 43205

1906 **GLASGOW, ALLEN M.; COTTON, ROBERT B.; & DHIENSIRI, KAMNUAL.** Reye Syndrome: III. The hypoglycemia. *American Journal of Diseases of Children*, 125(6):809-811, 1973.

The mechanism of hypoglycemia in Reye's syndrome was investigated by an evaluation of serum insulin and growth hormone levels, liver glycogen, and hepatic gluconeogenesis in patients with this syndrome. Glycogen was graded in biopsies from 39 patients with Reye's syndrome and 14 patients with acute encephalopathy of another origin. The glycogen from the Reye's syndrome patients was graded as absent in 14, decreased in 15, and normal in 10, which included 7 of the 9 survivors. Gluconeogenesis from pyruvate was markedly decreased in 2 patients with Reye syndrome as compared to animal controls. From the evidence, the hypoglycemia appears to be secondary to decreased hepatic glucose production; this supports the existing hypothesis that hepatic dysfunction is a primary disease mechanism in this disorder. (4 refs.) - *A. C. Schenker.*

1410 S. Dahlia St.
Denver, Colorado 80222

1907 **WERDER, EDMOND A.; & SONNABEND, WOLFGANG.** Neonatal infection with *Streptomyces pelletieri.* *American Journal of Diseases of Children*, 125(3):439-441, 1973.

A case of *Streptomyces pelletieri (S. pelletieri)* is described in a neonate whose mother was found to suffer from heavy vaginal discharge due to the same organism. During the course of illness, IgM levels in the serum were monitored; after the excessively high level at 3 weeks of age, a marked drop, even below the normal range, was observed. This appears to be the first instance of a proven infection due to *S. pelletieri* in a mother and her newborn baby. The pulmonary disease in the baby was diagnosed correctly after percutaneous lung puncture had been performed. Needle aspiration of lung exudate yielded the *S. pelletieri*. Treatment with penicillin proved to be clinically effective. (21 refs.) - *A. C. Schenker.*

Children's Hospital
Claudiusstrasse 6
9000 St. Gallen,
Switzerland

1908 **RICHMAN, DOUGLAS D.; ZAMVIL, LOUIS; & *REMINGTON, JACK S.** Re-

current Pneumocystis carinii pneumonia in a child with hypogammaglobulinemia. *American Journal of Diseases of Children*, 125(1):102-103, 1973.

The occurrence of 3 attacks of clinical *Pneumocystis* pneumonia in a child with hypogammaglobulinemia, each episode diagnosed by demonstration of the organism, suggested reactivation of latent infection. Each of the 3 episodes was characterized by the same clinical symptoms, which included fever, tachypnea, nonproductive cough, anorexia, lethargy, and diarrhea. Each episode radiographically had a diffuse interstitial infiltrate and bilateral hilar adenopathy, both of which resolved completely within 2 months of discharge. Eosinophilia was also present in each of the episodes. Demonstration of normally appearing *Pneumocystis* organisms in a lung aspirate obtained 3 days after his most recent course of therapy with pentamidine suggests chronicity of the infection. It was decided to initiate prophylactic therapy in this situation, although this is without precedent. (7 refs.) - *A. C. Schenker.*

Palo Alto Medical Research
Foundation
Palo Alto, California 94301

1909 **LANDRIGAN, PHILIP J.; MURPHY, KEVIN B.; MEYER, HARRY M.; PARKMAN, PAUL D.; EDDINS, DONALD L.; & WITTE, JOHN J.** Combined measles-rubella vaccines: virus dose and serologic response. *American Journal of Diseases of Children*, 125(1):65-67, 1973.

A clinical trial of several combinations of live measles and rubella vaccine was conducted with particular attention to whether there is any alteration in the pattern of antibody response effected by a change in the dose of a component, and whether attenuated measles or rubella virus is transmissible when given in combination. Attenuated measles vaccine and HPV-77 DE 5 rubella vaccine were combined in the field and given by single injection; 4 different dose mixtures were used, each of 2 lots of measles vaccine being combined with each of 2 lots of rubella vaccine. The results confirmed and extended previous studies as to the efficacy of selected combinations of the 2 vaccines. The seroconversion rates and the geometric mean titers of antibodies to each component were comparable to those obtained in previous trials of monovalent measles and rubella vaccines. There was no evidence of enhancement of the clinical response or of spread of the attenuated viruses to a small number of susceptible mothers of vaccinees. (12 refs.) - *A. C. Schenker.*

Center for Disease Control
Atlanta, Georgia 30333

1910 **CARAMIA, FELICE; DE BAC, CARLO; & *RICCI, GERMANO.** Virus-like particles within hepatocytes of Australia antigen carriers. *American Journal of Diseases of Children*, 123(4):309-311, 1972.

Electron microscopic studies on liver biopsies from both Australia (Au)-antigen-positive and Au-antigen-negative patients with and without clinical manifestations of acute hepatitis are reported. The presence of virus-like particles of 180 A in diameter in the liver of Au-antigen-positive Ss (all carriers of Au-antigen) is confirmed; these were found in Ss with no clinical or biochemical evidence of liver disease. Such particles were not seen in the cytoplasm of the same hepatocytes. The screening of liver biopsy specimens from 12 patients (8 with Au-antigen positive and 4 with Au-antigen negative sera) with acute hepatitis was negative; no particles of the same or different size were seen in the nucleus or cytoplasm. (13 refs.) - *A. C. Schenker.*

Universita di Roma
Policlinico Umberto I
00161 Rome, Italy

1911 **WILLS, EDWARD J.** Electron microscopy of the liver in infectious mononucleosis hepatitis and cytomegalovirus hepatitis. *American Journal of Diseases of Children*, 123(4):301-303, 1972.

The liver biopsy findings in two cases, one of infectious mononucleosis, and one of cytomegalovirus infection, as seen by electron microscopy, are described. The structural changes in these cases resemble infectious hepatitis in several aspects: dilated endoplasmic reticulum in infectious mononucleosis; an occasional cell was seen in the cytomegalovirus liver, suggesting that it may have been common in the early stage of the illness. In the cytomegalovirus infection, when jaundice had persisted for some time and was mainly of the obstructive type, the predominant changes were more typical of prolonged cholestasis infectious hepatitis, accumulation of bile pigment and dilated

bile canaliculi. A virus could not be identified in either case. (10 refs.) - *A. C. Schenker.*

Clinical Research Centre
Watford Rd., Harrow HAI, 3UJ
England

1912 **ROSS, CONSTANCE A. C.** Vaccination against rubella. *British Medical Journal*, 1(5792):109, 1972. (Letter)

A recommendation is made which is aimed at helping in the assessment of the problem of rubella embryopathy on the way to developing the most suitable policy regarding vaccination. Findings of a 4-year study (1966-1970) of congenital rubella infection suggest that severe embryopathy resulting from such infection is now rare, perhaps because of more precise identification of rubella infection during pregnancy and termination of pregnancy when required. Widespread attempts to identify and immunize all seronegative childbearing women would inevitably result in the occasional administration of vaccine unwittingly to some women in the early months of pregnancy. It would seem simpler and wiser to adopt a policy of careful serological testing of all pregnant women who have suspected rubella or are rubella contacts for current or recent rubella infection. (1 ref.) - *A. C. Schenker.*

Regional Virus Laboratory
Ruchill Hospital
Glasgow, Scotland

1913 **KUMAR, MARY L.; NANKERVIS, GEORGE A.; & *GOLD, ELI.** Inapparent congenital cytomegalovirus infection: a follow-up study. *New England Journal of Medicine*, 288(26): 1370-1372, 1973.

A follow-up study on 15 infants with inapparent congenital cytomegalovirus was conducted to assess the physical and mental development with increasing age; these infants had been previously described by Starr and coworkers. As judged by their physical and psychological examinations, the children with congenital inapparent cytomegalovirus were indistinguishable from their peers at age 4 years, except for one severely affected child who had a developmental level of less than 3 months. A mean IQ of 85.2 was obtained in the other 14 congenitally infected children, but the control group showed a similar level of intelligence. These low levels are apparently due to the fact that all these children were culturally disadvantaged. Urine cultures were positive for cytomegalovirus in 11 of the 15 congenitally infected children and 5 of these 11 showed a significant decrease in their cytomegalovirus complement fixation antibody titer as compared to the titers of sera obtained during the first 8 months of life. There is a possibility that subtle damages such as learning disabilities or loss of hearing may not become apparent until still later in life, in the infected children. (7 refs.) - *A. C. Schenker.*

*Cleveland Metropolitan
General Hospital
Cleveland, Ohio 44109

1914 **SABATH, L. D.; & ROSNER, B.** Susceptibility to meningococcal meningitis. *New England Journal of Medicine*, 288(22):1185, 1973. (Letter)

It is pointed out that a report on the effect of Group C vaccine in preventing Group C meningococcal meningitis which was stressed as being group specific and which mentioned that during the observation period the attack rate of B meningococcal meningitis was not diminished, is in fact not commensurate with the data. The figures shown for the rate of Group B attack were 0.291/1000/8 weeks, whereas the rate in the controls was 0.055.1000.8 weeks. Furthermore, the article did not deal with either the importance or the possible statistical significance of the increased attack rate of Group B disease in the immunized persons. It has not been apparent why meningococcal meningitis develops in some people while others carry meningococci in the nasopharynx without the development of frank disease. Meningococcal infection, and possibly other infections, may be the result of a challenge during a transient hypersusceptible period when the normal body defense is hampered by antibody to related antigens blocking access to the invader. (2 refs.) - *A. C. Schenker.*

Boston City Hospital
Boston, Massachusetts

1915 **WEINER, LESLIE P.; JOHNSON, RICHARD T.; & HERNDON, ROBERT M.** Viral infections and demyelinating diseases. *New England Journal of Medicine*, 288(21):1103, 1973.

Human demyelinating diseases associated with

viral infections; experimental diseases in which mechanisms of virus-induced demyelination are being investigated; and evidence for a viral etiology of multiple sclerosis, are reviewed. Although it is assumed that virus-induced demyelination is probably triggered by viral infection, such a mechanism has not been established. In progressive multifocal leukoencephalopathy and in JHM-virus infection of rodents, for example, myelin disruption appears to be the result of viral infection of the oligodendrocytes maintaining the myelin sheaths. The former disease usually develops in immunologically compromised patients, and demyelination in the latter disease is not inhibited by chemical immunosuppression. None of the demyelinating diseases currently attributable to viral infection follow the exacerbating and remitting course characteristic of multiple sclerosis. Recent serologic, virologic, and electron microscopical studies, directly implicating myxoviruses, have lent support to the theory of viral causation in the case of multiple sclerosis. (95 refs.) - *A. C. Schenker.*

Johns Hopkins School of Medicine
Baltimore, Maryland 21205

1916 **HANSHAW, JAMES B.** Congenital cytomegalovirus infection. *New England Journal of Medicine*, 288(26):1406-1407, 1973.

A paper by Kumar, Nankervis and Gold presents evidence that definite neurologic sequelae developed in only one of 15 infants born with this infection over a 4-year observation period. In Cleveland, 1.2% of infants were found to excrete cytomegalovirus at birth. The infant with microcephaly, intracranial calcifications and a developmental level of less than 3 months at 4½ years of age, described in the Cleveland series, is an example of the severest form of brain damage from this infection. If the data in this series are typical of other communities, cytomegalovirus infection could be responsible for a large percentage of the children with the most severe retardation. Evidence for the role of cytomegalovirus in the causation of mild mental retardation is incomplete; psychometric assessments in children from culturally disadvantaged communities are questionable. Mild degrees of neurologic dysfunction and retardation appear to be more common among the poor; these may be shown to be more socially important than the severe forms of brain damage. The concept that cytomegalovirus is a major factor in the latter case should not be discarded. (6 refs.) - *A. C. Schenker.*

1917 Rubella vaccination. *British Medical Journal*, 3(5822):305-306, 1972. (Editorial)

Rubella vaccines are reviewed in terms of reactions. The 3 vaccines used at present have a very low incidence of mild transient reactions in children, but adult females are more prone to reactions, particularly arthralgia, which commonly occurs in adults with natural rubella. The vaccines derived from HPV-77 virus are particularly apt to cause such reaction in adults. Children with brachial radiculoneuritis are awakened from sleep by paresthesia; it commonly lasts from 30 sec to 30 min and occurs 1-6 times a night over about a month. The aim of rubella vaccination is to protect the developing embryo from exposure to the rubella virus from the day of conception. This can be done by mass vaccination of the main disseminators of rubella infection in the community, primary school children, or by vaccination of all rubella-susceptible girls when they are about to reach child-bearing age. The risk of causing congenital rubella has not yet been surmounted by the various vaccine strains. (28 refs.) - *A. C. Schenker.*

1918 Herpes genitalis. *British Medical Journal*, 1(5795):264-265, 1972. (Editorial)

The effects of Herpesvirus hominis, type 2, isolated from the genital tract are described. There is growing evidence that this virus is venereally transmitted, occuring most often among women attending venereal disease clinics. Herpes genitalis tends to recur, and the lesions in the first infection are more marked and persist longer (2-6 weeks) than in subsequent attacks. The common site in males is the glans penis, prepuce, and shaft of penis, and in women the external genitalia and occasionally the cervix, where it can cause severe cervicitis with necrotic ulceration. There is evidence that a carrier state exists in women. A strong association between antibodies to herpesvirus type 2 and cervical neoplasia has been observed in Negro women. It has also been observed that antibody titers against this virus were significantly higher among patients with carcinoma of the cervix than in matched controls. The risk of infection to infants of mothers carrying the virus in late pregnancy is estimated as 60%. There are also reports of an association of

abortion or congenital malformation with infection early in pregnancy. (19 refs.) - *A. C. Schenker.*

1919 **ABBOTT, G. D.** Neonatal bacteriuria: a prospective study in 1,460 infants *British Medical Journal*, 1(5795):267-269, 1972. 1972.

The incidence of neonatal urinary infection was investigated in a representative population in New Zealand comprising 1,460 infants. Fourteen infants (11 males and 3 females) had bacteriuria, an incidence of 0.95%. Five of these infants failed to thrive; vomiting was seen in 3, fever in 2, diarrhea in one, convulsions in one, and jaundice in one. The remaining 9 were asymptomatic. The organisms identified from bladder puncture urine of the infants with asymptomatic bacteriuria were all *Escherichia coli*. In the infants with transient asymptomatic bacteriuria, the organisms found were *E. Coli, Staphylococcus aureus, Staph. epidermis* and the mixed infection with an Enterobacter species and Streptococcus viridans. Only one infant with bacteriuria had a positive blood culture; the organism identified from both blood and urine was a Klebsiella species. The blood urea was raised in 2 infants; pyuria occurred in 6 infants, and proteinuria in 3. (14 refs.) - *A. C. Schenker.*

Christchurch Hospital
Christchurch, New Zealand

1920 **TAN, K. L.; & CHAN, Y. C.** Immunoglobulin levels in newborn infants with hepatosplenomegaly. *British Medical Journal*, 1(5795):269-270, 1972.

Immunoglobulin determinations in newborn infants with hepatosplenomegaly are reported and the results suggest intrauterine infection in some of the infants. The 97 infants with hepatosplenomegaly were compared with 147 control infants for IgM and IgA; all were considered normal at birth and had no apparent disease. Increased IgM levels were found in 30% of the infants with hepatosplenomegaly; in the control group only 3% had increased IgM levels, a significant difference ($P<0.001$). The results suggest that intrauterine infections may be the cause of the hepatosplenomegaly. No difference was found in IgA concentrations in the 2 groups. (11 refs.) - *A. C. Schenker.*

University of Singapore
Singapore 3

1921 **DETELS, ROGER; MCNEW, JANE; BRODY, JACOB A.; & EDGAR, ANNE H.** Further epidemiological studies of subacute sclerosing panencephalitis. *Lancet*, 2(7819):11-14, 1973.

A case-control study and serologic investigation were conducted with 43 subacute sclerosing panencephalitis patients from various areas of the United States and 38 controls from the same communities matched for CA and sex, each selected by patients' mothers as being a close lifelong friend of the patient. Interviews stressed infectious diseases, exposure to sick and well animals, neurologic allergic illness, and familial diseases. Among the 43 patients, the median age of infection was 15 months among the 31 Ss with a positive measles history as compared with a median age of 48 months among the 22 controls with a positive history. Twelve patients and no controls had measles at less than 1 year of age. Six patients as compared with 1 possible instance among controls had measles within 6 months of chickenpox. An excess of allergic disease was reported for the parents and siblings of patients. History of neurologic disease was similar among first-degree relatives of patients. High titer to measles occurred only in patients and not in family members. Patients had more frequent exposure to animals. The data suggest that an unusual natural measles-virus infection is involved together with an additional factor existing among the population primed by an unusual measles infection, since the highest risk of florid panencephalitis is in rural males. (16 refs.) - *B. J. Grylack.*

U.C.L.A. School of Public Health
Los Angeles, California

1922 **PORTER, C. A.; MOWAT, ALEX P.; COOK, P.J.L.; HAYNES, D.W.G.; SHILKIN, K. B.; & WILLIAMS, ROGER.** $Alpha_1$-antitrypsin deficiency and neonatal hepatitis. *British Medical Journal*, 3(5824):435-439, 1972.

In the course of a survey of neonatal hepatitis, 5 instances of $alpha_1$-antitrypsin deficiency (ZZ phenotype) were found among the first 28 infants investigated; the variable course of hepatitis in these 5 cases is reported. All the infants had an acute hepatitis; because of its action as an enzyme-inducing agent, phenobarbitone was tried in 3 patients, but no increase in the $alpha_1$-antitrypsin serum levels resulted. The lack of any

effective form of therapy makes genetic counseling important. Parents of an affected child can be told that in subsequent pregnancies thay have a 1:4 chance of having a child with the homozygous-deficiency state, but guidance regarding the likelihood of the child's developing either liver or pulmonary disease cannot be given. There is no known method for detection of the deficiency in the amniotic fluid. (27 refs.) - *A. C. Schenker.*

King's College Hospital and Medical School
London, S.E.5, England

1923 **MOLSTED-PEDERSEN, LARS; TRAUTNER, HANS; & JORGENSEN, K. R.** Plasma insulin and K values during intravenous glucose tolerance test in newborn infants with erythroblastosis foetalis. *Acta Paediatrica Scandinavica*, 62(1):11-16, 1973.

Eighteen infants with erythroblastosis fetalis due to Rh immunization and 11 normal infants matched for birthweight were studied for plasma insulin values during i.v. glucose tolerance tests performed 3 hours after birth in the fasting state. The mean fasting plasma insulin concentration 3 hours after birth was significantly higher in the 18 Ss than in the 11 control infants (28 and 16 μunits/ml, respectively; t=3.29, p<0.005), and the insulin concentration remained significantly higher in these infants throughout the experimental period. Between birthweight and fasting insulin concentrations and between birthweight and K value significant positive correlations were found in the 18 Ss (r=0.52, t=2.35, pH0.05, and r=0.48, t=2.18, pH0.05). The fasting glucose concentration 3 hours after birth in the 18 Ss was correlated positively with the umbilical cord hemoglobin concentration (r=0.5, t=2.01, 0.05<p<0.1) and negatively with the cord bilirubin concentration at birth (r=0.67m t=3.39, p<0.005). The insulin response following i.v. glucose load was basically the same in the 2 groups, exhibiting an even increase and reaching a maximum in 40 to 60 minutes in the 18 Ss, but it differed from that in infants of diabetic mothers. Birthweight of the 18 Ss was normal in relation to their gestational age, unlike that of infants of diabetic mothers, who weigh approximately 550g more than do normal infants with a gestational age of 260 days. Thus, the hyperinsulinism in infants with erythroblastosis fetalis is probably etiologically different from that in infants of diabetic mothers. (24 refs.) - *B. J. Grylack.*

Rigshospitalet
2200 Copenhagen N., Denmark

1924 **DAYAN, A. D.; & STOKES, MOLLIE I.** Rapid diagnosis of encephalitis by immunofluorescent examination of cerebrospinal-fluid cells. *Lancet*, 1(7796):177-179, 1973.

An attempt to diagnose acute encephalitis in man by immunofluorescent examination of cerebrospinal fluid cells for viral antigens has demonstrated the value of this technique for the day-to-day confirmation of a diagnosis of viral encephalitis. Of 95 cases in which viral encephalitis was investigated, a correct diagnosis of encephalitis was made in 30 cases and of "not encephalitis" in 57 by immunofluorescence. Three incorrect diagnoses of "not encephalitis" were made, and 5 samples were unsuitable because of blood contamination. The relative simplicity and rapidity of this technique make it a worthwhile adjunct in the diagnosis of viral encephalitis. (5 refs.) - *B. J. Grylack.*

Wellcome Research Laboratories
Langley Court
Beckenham, Kent BR3 3BS, England

1925 **MOLLISON, P. L.** Clinical aspects of Rh immunization. *American Journal of Clinical Pathology*, 60(3):287-301, 1973.

The initiation of sensitization during pregnancy constitutes an important cause of failure to suppress Rh immunization. Studies indicate that approximately 70% of Rh-negative Ss exhibit a primary response to a single adequate dose of Rh-positive red cells, whereas these cells survive normally in the circulation of nonresponding Rh-negative Ss even despite repeated small transfusions given over a period of years. A dosage of 25 μg anti-Rh per ml Rh-positive erythrocytes seems to be fully effective for suppression of Rh immunization in Rh-negative Ss. Given that anti-Rh is present in the plasma of approximately 0.8% of Rh-negative women at the time of delivery of a first Rh-positive infant and that a dose of 250 μg administered at the time of the first delivery will suppress Rh sensitization in all but about 0.3% of women, the minimum failure rate of treatment should be in the vicinity of 1.9%. In fact, lower failure rates are being reported currently. Clinical

trials in progress in different countries should demonstrate whether or not injections of anti-Rh during pregnancy are feasible. In the meantime, the existing, simple method of treatment has been surprisingly successful. (59 refs.) - *B. J. Grylack.*

M.R.C. Experimental Haematology
Unit
St. Mary's Hospital Medical School
London W.2, England

1926 **CHRISTOPHER, P. J.** Measles immunization in Sydney. *Medical Journal of Australia*, 2(8):414-415, 1972.

A survey to determine the immunization status against measles was conducted with 1,383 children between CA 1 and 3 years in the Western Metropolitan Health District of Sydney, Australia. Of the 1,368 for whom previous measles or measles immunization could be established, only 221 (16.1%) had been vaccinated. Of the 1,147 unvaccinated children, 307 (26.8%) had had measles and 840 (73.2%) had not. Ten (4.5%) of the immunized children had also had measles, 3 of them having been in contact with a measles patient at the time of immunization and a fourth child being immunized at age 2 years 4 months, after having measles at 6 months. (7 refs.) - *B. J. Grylack.*

Western Metropolitan Health
District
307 Church Street
Parramatta, N.S.W. 2150,
Australia

1927 **THOMPSON, GEORGE R.; WEISS, JOSEPH J.; SHILLIS, JOAN L.; & BRACKETT, ROBERT G.** Intermittent arthritis following rubella vaccination. A three-year follow-up. *American Journal of Diseases of Children*, 125(4):526-530, 1973.

Thirty-nine of 40 children who suffered from arthritis after vaccination with the HPV-77-DK 12 rubella vaccine were reexamined 2 years following their arthritis, and their parents were questioned 3 years after vaccination. Of 11 children classed as having definite recurrence, 9 cases involved the knee (81%). Moreover, of the 18 children with some articular complaints, 14 had knee involvement (79%). During the initial attack of arthritis following vaccination, of the group of 40 children, the knee was involved in 26 cases (65%). In the 3-year period of follow-up, attacks seemed to become less frequent and, in most instances, to stop completely. Routine clinical laboratory studies were unrevealing. (19 refs.) - *B. J. Grylack.*

Wayne County General Hospital
Eloise, Michigan 48132

1928 **SIZONENKO, P. C.; VALLOTON, M. B.; TERRAZ, M.; & PAUNIER, L.** Childhood hypoglycemia: plasma glucose and renin response to 2-deoxy-d-glucose. A new diagnostic test for epinephrine insufficiency. *Acta Paediatrica Scandinavica*, 62(1):101, 1973.

The cellular glucopenia induced by 2-deoxy-d-glucose, a sugar analogue, in patients with sporadic hypoglycemia does not produce the epinephrine response seen in Ss without this condition. Administration of 2-deoxy-d-glucose to control children (CA 6 years 5 months to 8 years 7 months) was followed by clinical manifestations of increased secretion of epinephrine, and a secondary hyperglycemia and a rise of plasma renin activity were observed. Its administration to 5 children with similar CA presenting with idiopathic hypoglycemic episodes provoked no clinical symptom to epinephrine secretion and no increase in blood glucose or plasma renin activity. The results suggest that these patients may be affected by an absence of sensitivity of the autonomic nervous system to 2-deoxy-d-glucose or by a blockade in the efferent nervous pathways or the adrenal medulla. - *B. J. Grylack.*

1929 **ZURBRUGG, R. P.; SIDIROPOULOS, D.; & KASER, HANS.** Epinephrine and cortisol dysregulation in neonatal cerebral hemorrhage with hypoglycemia (NCHH). *Acta Paediatrica Scandinavica*, 62(1):100-101, 1973.

A study of 3 infants with neonatal cerebral hemorrhage with hypoglycemia (NCHH) involved demonstration of adequate endogenous adrenocorticotrophic hormone reserve and adrenal cortical function by vasopressin and synacthen tests, respectively, and evaluation of hypothalamic regulation of cortisol and epinephrine by insulin tolerance tests. Epinephrine response was virtually absent or insufficient in all Ss when first tested shortly after birth, and it became normal or

remained insufficient upon retesting 6 months, 1 year, and 18 months later. Similar results were found for the cortisol response, an insufficient response initially being followed by complete recovery or by either transitory or definitive fall to deficient values in the later course. Associated hypoglycemia may constitute a transitory or definitive impairment of hypoglycemia-sensitive centers for both epinephrine and cortisol regulation in infants with a cerebral hemorrhage affecting the hypothalamus. - *B. J. Grylack.*

1930 **OH, W.; YAO, A. C.; HANSON, J. S.; & LIND, J.** Peripheral circulatory response to phototherapy in newborn infants. *Acta Paediatrica Scandinavica*, 62(1):49-54, 1973.

Changes in peripheral circulation and temperature were explored in order to explain increased insensible water loss in newborn infants treated by phototherapy due to jaundice. Ss were 8 newborn infants with CA of 10 to 127 hours and birthweights of 1,490 to 3,950g. Calf blood flow (CBF) increased significantly ($p<.05$) to levels 30% to 80% above the control CFB average of 8.8+0.9ml/min/100g during the 30-minute phototherapy period and also decreased significantly ($p<0.05$) when phototherapy was turned off. A direct correlation between CBF and skin temperature measured simultaneously on the contralateral leg was observed with γ values of 0.724 and 0.588 at 15 and 30 min after phototherapy, respectively. At 15 and 30 min after phototherapy was turned on, the outer wall of the incubator became warmer by 1 to 2° C, respectively, and incubator air temperature decreased significantly, a drop possibly representing the compensatory mechanism of the servo control unit which shuts off the incubator warming device as epigastric skin temperatures rise slightly at 5 to 15 min after phototherapy. Respiratory rate increased significantly 5, 10, and 30 min after phototherapy was turned on and decreased significantly after it was stopped. (8 refs.) - *B. J. Grylack.*

Harbor General Hospital
UCLA School of Medicine
Torrance, California

1931 **NEWNS, G. H.** Endocrinopathies in thalassaemia major. *Acta Paediatrica Scandinavica*, 62(1):91, 1973 (Abstract)

Two patients with thalassemia major were reported to have developed diabetes mellitus and hypoparathyroidism. Both had growth retardation and showed no signs of puberty. One patient, aged 22 when she died, had received transfusions at approximately 6-week intervals since age 18 months, and the second patient, aged 17 years, had received frequent transfusions at 6- to 8-week intervals since age 19 months. At autopsy, extensive deposits of hemosiderin were found in the pituitary, adrenal glands, pancreas, liver, and heart muscle in the first patient. Such massive deposits in the endocrine glands may lead gradually to destruction of the secretory cells, with consequent partial or total loss of endocrine function. - *B. J. Grylack.*

1932 **RUBALTELLI, F. F.; & LARGAJOLLI, G.** Effect of light exposure on gut transit time in jaundiced newborns. *Acta Paediatrica Scandinavica*, 62(2):146-148, 1973.

The Carmine Red test was performed on 13 full-term healthy newborns, 12 full-term jaundiced newborns before and during phototherapy, and 10 full-term healthy newborns who were subjected to phototherapy. The speed of complete intestinal transit in the first group was 13.14+4.43 hours. Intestinal transit time was normal in the second group before phototherapy but was accelerated after treatment. Phototherapy appeared to have no effect on intestinal transit time in healthy newborns. The findings indicate that therapeutic exposure of jaundiced newborns to light provokes an increased rate of intestinal transit and the appearance of loose green stools, as compared with normal and jaundiced newborns not exposed to therapy. The diarrhea which occurs in infants during phototherapy seems to result from the biliary elimination of photodecomposition derivatives of bilirubin. (8 refs.) - *B. J. Grylack.*

University of Padova
Padova, Italy

1933 **ZOUMBOULAKIS, D.; ANAGNOSTAKIS, D.; ARSENI, A.; NICOLOPOULOS, D.; & MATSANIOTIS, N.** Gentamicin in the treatment of purulent meningitis in neonates and infants. *Acta Paediatrica Scandinavica*, 62(1):55-58, 1973.

Gentamicin was administered to 8 neonates and 13 infants under 8 months of age suffering from purulent meningitis who had failed to improve

after a 5- to 6-day parenteral course of ampicillin, alone or in combination with kanamycin in appropriate doses. Medication was successful in 18 of 21 cases, the infection being controlled within 2 to 5 days. Of the remaining 3, 2 died and 1 developed hydrocephaly. Recovery was complete and permanent in all successfully treated cases. There were no relapses nor any evident toxic effects of the drug, and follow-up of 13 infants showed continued good health. (13 refs.) - *B. J. Grylack.*

University of Athens
"St. Sophie's" Children's
Hospital
Goudi, Athens 608, Greece

1934 **BARTSOCAS, CHRISTOS S.; & PANTELAKIS, STEFANOS N.** Human growth hormone therapy in hypopituitarism due to tuberculous meningitis. *Acta Paediatrica Scandinavica*, 62(3):304-306, 1973.

Two females with short stature due to growth hormone deficiency following treatment of tuberculous meningitis in early childhood showed adequate growth response to administration of human growth hormone. In 1, hormone therapy resulted in a height increase of 8 cm in 13 months, and the second grew from 128 cm to 136.1 cm following six months' treatment. Long-term supervision of children treated for tuberculous meningitis is important in order to detect the onset of the endocrine sequelae, which may not be evident immediately. (18 refs.) - *B. J. Grylack.*

3 Kapsali Street
Athens 138, Greece

1935 **GUPTA, J. D.** Rubella-specific IgM antibody as an aid to diagnosis. *Lancet*, 2(7825):379, 1973. (Letter)

For serologic diagnosis, presence of rubella-specific immunoglobulin (Ig) M may be sought only if it is not possible to demonstrate a rise in antibody titer in paired sera collected 7 to 14 days apart and tested simultaneously. A test for IgM antibody in low-titer sera collected early in the illness may be used as a quick diagnosis, but testing of a second sample will be necessary if the result is negative. Past experience with the testing of many sera from naturally infected and vaccinated individuals had shown the feasibility of demonstrating specific IgM antibody in serum samples collected after primary infection or successful vaccination. Only such situations as testing several weeks after the illness and cases of reinfection might necessitate more sensitive methods for detecting rubella-specific IgM. (4 refs.) - *B. J. Grylack.*

Children's Medical Research
Foundation
Royal Alexandra Hospital for
Children
Camperdown, N.S.W. 2050, Australia

1936 **EMOND, R.T.D.; & MCKENDRICK, G.D.W.** Tuberculosis as a cause of transient aseptic meningitis. *Lancet*, 2(7823):234-236, 1973.

The spontaneous recovery from tuberculous meningitis is described in 4 patients. The nature of the illness in 2 of the patients would never have been recognized without routine culture for tubercle bacilli. In both patients recovery was rapid and no other evidence of tuberculosis could be found. In the third patient, there were some apparent features of tuberculosis, but these were not considered sufficient to warrant immediate treatment, and recovery took place uneventfully. It seems unlikely that 2 doses of streptomycin and p-aminosalicylic acid with isoniazid played any part in this recovery. The fourth patient, who was suspected of having disseminated lupus erythematosus (later confirmed), had positive tuberculin tests and a slight deterioration in the cerebrospinal fluid (CSF). When a positive culture is obtained from a patient who has made a spontaneous recovery, chemotherapy is not necessary as a routine. (4 refs.) - *A. C. Schenker.*

Royal Free Hospital
London WC1, England

1937 **LONGSON, MAURICE; LIVERSEDGE, L. A.; & WILKINSON, I.M.S.** Diagnosis of virus encephalitis. *Lancet*, 1(7797):397, 1973. (Letter)

A report by Dayan and Stokes on the diagnosis of virus encephalitis by immunofluorescent technique applied to cerebrospinal fluid (CSF) must not be confused with diagnosis of herpes encephalitis, which can be made only by brain biopsy. The isolation of Herpesvirus h-simplex from lumbar fluid is extremely rare, and the presence of stainable antigen in CSF lymphocytes in the absence of infectious virus seems unlikely. In 11

proven cases of herpes encephalitis, the virus has been successfully stained by immunofluorescence in brain tissue, but there was no evidence of its antigenic presence in lumbar fluid, although the culture of the CSF from 1 of these 11 cases proved positive. Until the procedure of Dyan and Stokes is established beyond doubt, diagnostic brain biopsy and possible therapeutic decompression should be performed. (3 refs.) - *A. C. Schenker.*

Manchester Royal Infirmary
Oxford Road, Manchester M13 9WL,
England

1938 **STEVENSON, J.** Bacterial meningitis and tuberculous meningitis. *British Medical Journal*, 2(5863):411-414, 1973.

The morbidity from bacterial meningitis is discussed, including diagnosis, treatment, and prophylaxis. Diagnosis should be made early; the most common symptoms are: malaise with fever, headache, vomiting, and generalized aching. Meningitis is often confused with other conditions, because of the early nonspecific signs; many cases are considered primary in that no local focus of infection is found, but in others invasion of the meninges results from a mechanical breach of the defense mechanisms. Meningococcal, H. influenzae, pneumococcal, tuberculous, and neonatal types of meningitis are described. The definitive diagnosis and treatment of meningitis are essentially hospital exercises. The basic principles of treatment include: antibiotic treatment wherever possible, guided by the isolation of the responsible organisms; where antibiotic penetration is poor, intrathecal therapy is justified at the acute stage of the illness. Supportive treatment includes skilled nursing; when necessary, anticonvulsant therapy; and corticosteroids. The most serious complications in meningitis are acute obstructive hydrocephaly and subdural effusions. Meningococcal infection provides the greatest danger, and prophylaxis among contacts should be observed. Prophylaxis with penicillin has been successful with the pneumococcal variety. (9 refs.) - *A. C. Schenker.*

Seacroft Hospital
Leeds LS14 6UH, England

1939 **SKOLDENBERG, BIRGIT; JEANSSON, STIG; & WOLONTIS, SIGVARD.** Herpes simplex virus Type 2 in acute aseptic meningitis. *British Medical Journal*, 2(5866):611, 1973. (Letter)

With respect to central nervous system (CNS) invasion by herpes simplex, Type 2, a number of studies are mentioned and a report of 7 patients is presented. In a Washington study, covering a 25-year period, 49 cases of herpes simplex virus (HSV) infection of the CNS were observed. In a Stockholm study covering a 10-year period, of 3,117 cases of acute aseptic infection of the CNS, 17 cases of HSV infection were found. In the discussion of the latter study, the hypothesis was proposed that one type of HSV can cause encephalitis and another type meningitis. This hypothesis is supported by the report of 7 patients, treated for acute aseptic meningitis, from whose CSF specimens HSV were isolated. All 7 CSF strains were identified as HSV type 2 by immunoelectro-osmophoresis with type-specific rabbit immune sera. The clinical picture of HSV Type 2 meningitis in these patients differed completely from that of herpes encephalitis. (8 refs.) - *A. C. Schenker.*

Roslagstull Hospital for Infectious
Diseases
Karolinska Sjukhuset, Sweden

1940 **SAVAGE, M. W.; MOOSA, A.; & GORDON, R. R.** Maternal varicella infection as a cause of fetal malformations. *Lancet*, 1(7799):352-354, 1973.

The case of an infant born with defects which on clinical grounds were judged to be the result of maternal varicella infection during the first trimester of pregnancy is presented. The clinical features are similar to 2 other reports, and the fetal structural malformation is undoubtedly due to the maternal varicella infection. The constant features are the reduction deformity of a limb and the distribution of skin scars along the length of the hypoplastic limb. Additional features in other cases include low birthweight, Horner's syndrome, chorioretinitis, dysphagia, and meningoencephalitis. The affinity of the varicella-zoster for the nervous system provides a logical explanation for the lesions occurring in the present case. The raised IgM level in this patient strongly suggests intrauterine infection. (8 refs.) - *A. C. Schenker.*

Radcliffe Infirmary
Oxford, England

1941 **NISHIMURA, C.** Antigenic relation of S.M.O.N.-associated virus to herpesvirus group. *Lancet*, 1(7795):159, 1973. (Letter)

The virus associated with subacute myelo-opticoneuropathy (SMON) is possibly a new member of the herpesvirus group. This presumption is based on the fact that many neurotropic herpesviruses grow preferentially in the central nervous system, travelling along nerves from the periphery, as does the SMON-associated virus, and occasionally cause recurrent infection. Serological tests with chorioallantoic-membrane (CAM) homogenates showed a complement-fixing antigen common to both SMON and herpes-simplex viruses, but the neutralizing antigens did not cross-react with each other. The finding suggests that SMON has a group-specific complement-fixing antigen in common with the herpesvirus group, but that its type-specific neutralizing antigen is different. (3 refs.) - *A. C. Schenker.*

School of Pharmaceutical Sciences
Kitasato University
Tokyo, Japan

1942 **DAVIES, MORGAN.** Subclinical lead poisoning. *Lancet*, 1(7796):205-206, 1973. (Letter)

The biological threshold limit value for blood lead to 80 microgm/100ml is considered a high threshold from the medical viewpoint. The value was fixed following extensive experience of the blood-lead test in industry in the USA. The World Health Organization has recommended a lowering of this figure to 70 microgm/100ml to increase the margin of safety of lead workers. Where blood levels approach or exceed such values, engineering action msut be taken to minimize the emissions of lead. - *A. C. Schenker.*

Fowler Davies & Co.
Foresters, Colgate
Horsham, Sussex RH12 4SY
England

1943 **DIRLING, D. J.; SCOPES, J. W.; & WIGGLESWORTH, J. S.** Babies born alive after intrauterine transfusions for severe rhesus haemolytic disease. *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 79(6):565-574, 1972.

Of 52 babies born alive following intrauterine transfusions for severe rhesus hemolytic disease during a 7-year period, exchange transfusions were performed in all but 2 babies, who died at age 1 hour and 45 minutes, respectively, and other major problems were encountered in all but 5. Of the total, 30 survived, 6 of whom were hydropic at birth. The primary problems affecting the infants at birth were severe birth asphyxia (34 of 52), hydrops fetalis (21 of 52), anemia (29 of 52), and hypothermia (21 of 52). During the neonatal period, 23 of 52 developed respiratory problems, and most of the babies at some time showed a certain degree of generalized neurological disturbance, with 6 of them manifesting specific and localized abnormalities. Anemia was the problem encountered most frequently at follow-up. Most of the surviving babies were found to be developing normally. (24 refs.) - *B. J. Grylack.*

M.R.C. Tuberculosis and Chest Diseases Unit
Brompton Hospital
London, England

1944 **ROVEY, L. A. DERRICK.** The use of anti-D gamma globulin for the prevention of Rh immunization. Results in 546 subsequent pregnancies in the Leeds region. *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 79(2):107-112, 1972.

Six months' follow-up of 2,865 women receiving anti-D gamma globulin in the Leeds region of England revealed a failure rate of 0.55% among 2,319 and a rate of 1.6% among the 546 who had a subsequent pregnancy in which the infant was Rh D-positive. In all 7 cases of Rh D-positive infants, the hemolytic process was mild, not a single child requiring an exchange transfusion. Of the 7 cases in which an Rh antibody was detected by papain technique only, prior to injection, 3 have had a subsequent pregnancy. Antibodies were detected during all 3 pregnancies but never above a level of 0.2 μg of anti-D, and direct antiglobulin tests were positive in 2 of 3 cases. No significant correlation was found between the failure rate, Kleihauer count, and dose of anti-D administered. Thus, although there was evidence of large fetal bleeds, a single dose of

anti-D appeared to give protection in some instances. (17 refs.) - *B. J. Grylack.*

Regional Transfusion Centre
Leeds, England

1945 **FAIRWEATHER, D.V.I.; BILLEWICZ, W.; LORAINE, J. A.; & BELL, E. T.** Endocrine function in rhesus isoimmunization. *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 79(2):97-106, 1972.

Serial estimations of estrone, estriol, pregnanediol, and human chorionic gonadotrophin (HCG) in maternal urine from 32 weeks' gestation until delivery in 89 rhesus immunized patients having infants affected by varying degrees of hemolytic disease or having stillbirths found at autopsy to be due to rhesus isoimmunization were compared with similar findings for a control group matched for CA and gestational period. A bioassay technique was employed. There was a tendency for urinary HCG readings to be higher than normal in rhesus cases, but no clear relationship was found between the titer and the degree of severity of the condition. Moreover, no definite correlation could be demonstrated between urinary HCG levels and placental weight. (23 refs.) - *B. J. Grylack.*

University College Hospital Medical School
London, England

1946 **IRWIN, GILBERT R., JR.** Cerebrospinal fluid pH and respiratory rate in bacterial meningitis. *Diseases of the Nervous System*, 33(4):276-279, 1972.

Measurement of the pH of cerebrospinal fluid and arterial blood in patients with meningitis due to *Diplococcus pneumoniae* showed a correlation of the change in the pH of arterial blood and cerebrospinal fluid with respiratory rate. The respiratory rate was elevated only in patients with a decreased cerebrospinal fluid pH. A corresponding relative alkalosis of the arterial blood was observed in all cases where the cerebrospinal fluid pH was decreased. The clinical severity of the disease was also related directly to a decreased cerebrospinal fluid pH. It appears that respiratory rate increases as the cerebrospinal fluid pH is lowered by the accumulation of cells, bacteria, lactic acid, and other metabolites or toxic products. If the process is a prolonged or severe one, respiratory arrest may occur. (9 refs.) - *B. J. Grylack.*

Yale School of Medicine
New Haven, Connecticut 06510

1947 **FELDMAN, LAWRENCE A.; RAINE, CEDRIC S.; SHEPPARD, RACHEL D; & BORNSTEIN, MURRAY B.** Virus-host cell relationships in meales-infected cultures of central nervous tissue. *Journal of Neuropathology and Experimental Neurology*, 31(4):624-638, 1972.

Cultured hamster cerebellum inoculated with the Edmonston strain of measles virus for up to 72 days produced infectious virus continuously throughout a 68-day period. Infectious virus was recovered form these cultures without the aid of the co-cultivation technique needed to isolate measles virus from cultures obtained from subacute sclerosing panencephalitis (SSPE) patients. Strain differences between SSPE and Edmonston virus may account for the distinction between viral production in Edmonston as opposed to SSPE cultures. SSPE cultures contain measles virus in a hidden or masked form, whereas Edmonston cultures synthesize infectious virus continuously. However, the absence of a nonspecific measles virus inhibitor in brain tissue infected with measles could explain the viral recovery reported here. The increased antibody levels to measles virus may be related to the inability to isolate infectious virus without using co-cultivation techniques. (26 refs.) - *B. J. Grylack.*

New Jersey Medical School
Newark, New Jersey 07103

1948 Massachusetts Department of Public Health. Prevention of maternal sensitization of the Rh factor. *New England Journal of Medicine*, 287(4):197-198, 1972.

A statewide program to promote the full appropriate use of $Rh_0(D)$ immune globin among $Rh_0(D)$-negative mothers who have delivered $Rh_0(D)$ positive infants is being developed in Massachusetts. The immune globin is obtained from $Rh_0(D)$-negative donors who have acquired primary sensitization naturally or through blood transfusions. The donors receive booster

injections of hepatitis-free $Rh_0(D)$ positive blood as needed. The globulin solution is prpared from plasma by the Cohn cold-ethanol process and contains approximately 350 micrograms/ml of anti-$Rh_0(D)$. None of 610 $Rh_0(D)$ negative mothers receiving the immune globulin within 72 hrs of the delivery of an ABO compatible, $Rh_0(D)$ positive baby showed evidence of sensitization when they were examined 3 to 6 mo later. The immune globulin can be obtained from Biological Laboratories, Massachusetts Dept. of Public Health, 375 South Street, Boston 02130. (2 refs.) - *V. J. Goldberg.*

Massachusetts Dept. of Public Health
480 Tremont Street
Boston, Massachusetts 02116

1949 **KLASTERSKY, J.; CAPPEL, R.; SNOECK, J. M.; FLAMENT, J.; & THIRY, L.** Ascending myelitis in association with herpes-simplex virus. *New England Journal of Medicine*, 287(4):182-184, 1972.

A patient with ascending myelitis represents an instance where herpes-simplex virus (HSV) was associated with progressive spinal dysfunction. At autopsy, all levels of the spinal cord were necrotic, no intranuclear inclusions were found, and there were no signs of meningitis. The CSF was purulent and hypoglycorrhachiac but no tuberculosis bacilli (which are typically associated with these findings) or other bacteria were found in the CSF. The increased levels of neutrophils in the CSF may have reflected the acute necrosis of the nervous tissue. HSV type 1 was discovered in the CSF, indicating that this was the infectious agent. (6 refs.) - *V. J. Goldberg.*

Institut Jules Bordet
1000 Bruxelles, Belgium

1950 **ROCHE, J. K.; & STENGLE, J. M.** Clinical trials of hepatitis B immune globulin. *New England Journal of Medicine*, 287(5):251-252, 1972. Editorial.

The National Blood Resource Branch of NHLI initiated clinical studies to evaluate the efficacy of hepatitis B immune globulin (HBIG) in the prevention of treatment of hepatitis type B among those with known parenteral exposure to hepatitis B antigen (HBag), patients and staff in chronic renal dialysis units, and patients with acute fulminating hepatitis. There are 28 medical schools participating in the controlled, double-blind study. Since the presence of HBag in donor blood is one of the most important factors associated with the risk of hepatitis, the effects of a high titer of HBIG should be evaluated. If passively acquired immunity proves to be effective, its value for blood bank personnel, transfused patients, and others at risk of hepatitis would be great. A policy board composed of medical and lay members is empowered to halt the trial in the event of adverse effects. (13 refs.) - *V. J. Goldberg.*

1951 **ALTSHULER, GEOFFREY.** Toxoplasmosis as a cause of hydranencephaly. *American Journal of Diseases of Children*, 125(2):251-252, 1973.

The importance of placental examinations in the case of neonatal illness or death is demonstrated in a fatal case of congenital toxoplasmosis. Autopsy results established that the infant had hydranencephaly, myocarditis, interstitial pancreatitis, portal fibrosis and triaditis in the liver, interstitial nephritis, old microinfarcts in the adrenal glands, necrotizing retinochoroiditis, and toxoplasma cysts. Placental findings included hydrops associated with toxoplasmosis, abundance of Hofbauer cells, vascular proliferation in the placental villi, and pathognomonic cysts. Toxoplasmosis as a cause of hydranencephaly is thus a phenomenon which should be considered as equally important as recognized vascular factors. (9 refs.) - *C. Wares.*

Children's Hospital Medical Center
Cincinnati, Ohio 45229

1952 **GILL, THOMAS J.** Mechanisms of fetal immune response. *New England Journal of Medicine*, 287(10):518, 1972. (Letter)

The authors respond to the investigation by Aase et al. with a description of his studies relevant to this topic. In rats, immunization of the mother with a particulate antigen could sensitize the first and second litters of the F_1 generation and the first litter of the F_2 generation without further exposure to the antigen. The sensitization of the fetal lymphocytes may have been due to the passage of antigen from the mother to the fetus. Methods can be developed by which manipula-

tion of the maternal environment during fetal development could afford the offspring enhanced immune response. (4 refs.) - *V. J. Goldberg.*

University of Pittsburgh School of Medicine
Pittsburgh, Pennsylvania

1953 **COHEN, BENJAMIN E.** Mechanisms of fetal immune responses. *New England Journal of Medicine*, 287(10):517-518, 1972. (Letter)

With regard to the study by Aase on the lack of immunity conferral from mumps afflicted mothers to newborns, a suggestion was made in a later editorial that the mechanism in question may involve a mode of split intolerance. The author reports that an animal model exists in the guinea pig, where humoral immunity against dinitro-phenol (DNP)-albumin could be abrogated while cellular immunity was preserved by pretreating the animal with DNP-*D*-GL (a DNP conjugate with *D*-glutamic acid and *D*-lysine copolymer). The bone-marrow derived lymphocytes may be more susceptible to tolerance induction. It is possible that a similar state of split tolerance exists among Aase's Eskimo subjects. - *V. J. Goldberg.*

National Institute of Allergy and Infectious Diseases
Bethesda, Maryland

1954 **LEVY, NELSON L.** Synergism between polyoma and inactivated Sendai virus in human astrocytes, fibroblasts and HeLa cells. *Journal of Neuropathology and Experimental Neurology*, 31(4):639-644, 1972.

An experimental reproduction of the synergism proposed between paramyxovirus and papovavirus particles in cases of subacute sclerosing panencephalitis was achieved with polyoma and noninfectious paramyxovirus I (Sendai virus). When normal human astrocytes were fused by Sendai virus in the presence of polyoma, replication of the polyoma and extensive cytolysis took place in cultures of the fused cells. When similar experiments were carried out with human skin fibroblasts or HeLa cells, polyoma replication but no cytolysis was observed. Whereas the present experiments employed high concentrations of inactivated Sendai virus to promote fusion, the use of low concentrations of infectious paramyxoviruses to induce fusion is more consistent with a pathogenetic role for cell fusion in the intact animal. A synergistic interaction between the papovaviruses and the paramyxoviruses might account for various human disease processes. (10 refs.) - *B. J. Grylack.*

Duke University Medical Center
Durham, North Carolina 27710

1955 **WASHINGTON, JUAN L; BROWN, ARCHIE W., JR.; & STARRETT, ANDREA L.** The question of diarrhea and phototherapy. *Pediatrics*, 49(2):279-280, 1972.

Among 600 infants with a birthweight of less than 2,268g, 13 (17.1%) of the 76 infants receiving a minimum of 24 hours of phototherapy during the first 7 days of life had at least 1 episode of diarrhea as compared with 55 (14.8%) of the 371 infants who received no phototherapy at any time. The difference in the incidence of diarrhea in these 2 groups was not significant (X^2=0.09). (4 refs.) - *B. J. Grylack.*

Charity Hospital
New Orleans, Louisiana 70140

1956 **VAHERI, ANTTI; VESIKARI, TIMO; OKER-BLOM, NILS; SEPPALA, MARKKU; PARKMAN, PAUL D.; VERONELLI, JORGE; & ROBBINS, FREDERICK C.** Isolation of attenuated rubella-vaccine virus from human products of conception and uterine cervix. *New England Journal of Medicine*, 286(20):1071-1074, 1972.

Evaluation of various specimens, including the products of contraception, from 29 women who received HPV-77 DK-12 rubella vaccine and 6 women who received HPV-77 DE-5 vaccine and had legal abortions 11 to 30 days later indicated a hazard of placental and fetal invasion by the virus. Seroconversion was seen in all 24 initially susceptible vaccinated women. Of the 11 patients with low prevaccination antibody titers, 5 demonstrated a fourfold or greater rise in serum hemagglutinin-inhibition antibody titer. The only clinical reaction to the vaccine involved the joints. Rubella virus was recovered from the placenta in 6 cases, from the fetus in 1 case, and from 13 of 22 uterine cervical swabs obtained from the susceptible group. The failure to isolate virus from any of

the 11 vaccinated women with low prevaccination antibody titers indicated that even low levels of immunity could afford protection. The evidence underlines the need for vaccination of postpuberal women to be undertaken with extreme caution. (25 refs.) - *B. J. Grylack.*

Department of Virology
University of Helsinki
Helsinki, Finland

1957 **FRIEDE, REINHARD L.** Subpial hemorrhage in infants. *Journal of Neuropathology and Experimental Neurology*, 31(3):548-556, 1972.

Nine cases of subpial hemorrhage characterized by hematomas dissecting underneath the pia mater without evidence of hemorrhage into the subarachnoid space or into the brain parenchyma, 8 of them occurring in newborns and the ninth in a 13-month-old child, were collected from autopsies performed over a 6-month period on about 800 infants. There was approximately a 4% incidence of subpial hemorrhage. The basic features of the lesions were identical for all 9 cases. The hemorrhages were often bilateral, 4 being found in the cerebellum and 5 in the cerebral hemispheres over the temporal and parietal lobes. These subpial hemorrhages may represent a variant of the common type of asphyctic subarachnoid hemorrhage of newborns, but they possess their own characteristic morphology and pathogenesis. Subpial hemorrhages are more severe than the subarachnoid type. If survived, subpial hemorrhages are difficult to resorb and may be a cause of superficial cerebral siderosis. (18 refs.) - *B. J. Grylack.*

Case Western Reserve University
Cleveland, Ohio 44106

1958 **NORRIS, FORBES H., JR.** An ultrastructure study of herpes simplex virus encephalitis. *Journal of Neuropathology and Experimental Neurology*, 31(4):611-623, 1972.

A study of herpes simplex virus encephalitis produced by intracerebral virus inoculation of newborn brown and white Swiss mice revealed susceptibility of the neurons, astrocytes, and oligodendrocytes to the infection, whereas virus infection was infrequent in the microglia. Excessive nuclear folding, granual alteration of the chromatin, and dilatation of the endoplasmic reticulum appeared to be early virus-induced alterations in cells containing no visible virus. Enveloped and naked virions were found in the cytoplasm. The virus was detected frequently in the cytoplasm of macrophages, occasionally in pericytes, and sometimes in leukocytes. Only 2 infected endothelial cells were found in the course of the investigation. No endothelial aggregates were observed, but similar tubules were seen on occasion in oligodendrocytes. Astrocytic fibrillar bundles were often absent in cells loaded with virus. The present model is notable not only for the rarity of reduplication of the nuclear membrane but also for numerous areas of extensive folding of this membrane, which manifested unenveloped virus particles. (25 refs.) - *B. J. Grylack.*

Pacific Medical Center
San Francisco, California 94120

1959 **LOGOTHETIS, JOHN; CONSTANTOULAKIS, MATHIOS; ECONOMIDOU, IOANNA; STEFANIS, COSTAS; HAKAS, PAVLOS; AUGOUSTAKI, OLGA; SOFRONIADOU, K.; *LOEWENSON, RUTH; & BILEK, MARY.** Thalassemia major (homozygous beta-thalassemia): a survey of 138 cases with emphasis on neurologic and muscular aspects. *Neurology*, 22(3):294-304, 1972.

The neurologic status and intellectual and physical development were investigated in 138 patients with homozygous β-thalassemia (77 males, 61 females, aged 2-28 years). Common systemic features included frequent epistaxis; frequent infections (mostly respiratory); hepatitis; pathological fractures; abdominal pain; recurring low-grade fever; and major cardiopulmonary complications; these symptoms were seen in from 9-46% of the patients. The mean hemoglobin value was 7±1.5 gm%. Intelligence scores in 125 patients were within the range of the normal Greek control group. EEG data were obtained from 31 patients; in 22 patients, with a mean age of 9.5 years, there was a diffuse slowing. Myalgia was reported by 32 Ss, 6 with muscular weakness; the pain was intermittent and localized mostly in large muscles. In 45 patients there was evidence of reduced muscle mass. Difficulty in walking was found in 26 patients, the most consistent findings being a waddling gait, proximal weakness in the legs, and a positive Gowers' sign. MR was not a feature of this

disease, despite chronic anemia. Transient neurologic manifestations of an ischemic cerebrovascular nature were expressed as dizziness, visual blurring, and fainting; these improved after transfusion. Skeletal abnormalities paralleled the magnitude of osseous changes. (45 refs.) - *A. C. Schenker.*

University of Minnesota Medical
School
Minneapolis, Minnesota 55455

1960 **VYAS, G. N.; RAO, K. R.; & IBRAHIM, A. B.** Australia antigen (hepatitis B antigen): a conformational antigen dependent on disulfide bonds. *Science*, 178(4067):1300-1301, 1972.

Studies of structure and composition of hepatitis B antigen revealed that the reduction and alkylation of the disulfide bonds of the cystine residues by B-mercaptoethanol or diethiothreitol, followed by idoacetamide alkylation, resulted in complete loss of antigenic activity. Hepatitis B antigen was purified from the plasma of a healthy carrier by isopycnic banding and rate sedimentation on cesium chloride gradients. A solution of reduced and alkylated hepatitis B antigen tested by analytical ultracentrifugation showed a single band with a 31 S sedimentation coefficient. Testing for a possible subunit structure by chromatographic separation with Sephadex produced no signs of subunits. The antigen was treated with various chemical agents and dialyzed against NaCl before being tested with antiserum to hepatitis B antigen by countercurrent electrophoresis and hemagglutination inhibition. The results suggest that conformation of the antigenic determinant is critically dependent upon the disulfide bonds of the protein moiety. The immunogenicity of reduced and alkylated hepatitis B antigen was tested in 4 guinea pigs and compared with 4 other animals injected with purified native hepatitis B antigen. The animals immunized with reduced and alkylated antigen showed no detectable serological activity against the native molecule. (12 refs.) - *A. C. Schenker.*

University of California School
of Medicine
San Francisco, California 94122

1961 Breast milk and E. Coli. *Nature*, 235(5335):198, 1972. (Letter)

A specific inhibitory effect on *E. coli* by human milk has recently been reported by Bullen and Rogers of the National Institute for Medical Research, Mill Hill, and by Leigh of the Rowett Research Institute, Aberdeen. The investigators found in *in vitro* experiments that lactoferrin alone added to *E. coli* reduced the viable count to one-fiftieth of the control, and the addition of *E. coli* antiserum slightly reduced the viable count. Used together, however, the viable count was reduced to about one three-thousandth of the control. Human milk gave comparable results in the same series of experiments. It seems that the iron-binding properties of lactoferrin are responsible for this effect. The inhibitory effect of lactoferrin with specific antisera operates to keep down *E. coli* for the first few days after birth until the bowel has been well colonized with Lactobacilli. Gastroenteritis is less common in babies who are breast fed for these reasons. - *A. C. Schenker.*

1962 **NEEDLEMAN, HERBERT L.; TUNCAY, ORHAN C.; & SHAPIRO, IRVING M.** Lead levels in deciduous teeth of urban and suburban American children. *Nature*, 235(5333):111-112, 1972.

The exfoliated primary teeth of children exposed to lead absorption were analyzed for lead, in order to discover whether such analysis is a better indicator for storage of lead in calcified tissues than blood levels in these Ss. Sixty-nine deciduous teeth were collected from dental clinics serving children in the "lead belt" of urban Philadelphia, and 40 deciduous teeth were obtained from dentists in suburban areas. Dental amalgam and carious tissue were removed from the teeth, and the powdered bone was treated with perchloric acid to dissolve the inorganic components and precipitate dental proteins. Further treatment concentrated the lead in the organic phase, in which it was determined on an EEL 140 atomic absorption spectrophotometer. The mean tooth lead for suburban controls was 11.1 ± 14.8 ppm and for children from the ghetto 51.1 ± 109.0 ppm; the difference was significant ($p<0.01$). The findings suggest that deciduous teeth can be used as an indicator of lead intake and possibly of other trace elements in children. (3 refs.) - *A. C. Schenker.*

Harvard Medical School
Boston, Massachusetts

1963 **BEN-PORAT, TAMAR; & KAPLAN, ALBERT S.** Studies on the biogenesis of herpesvirus envelope. *Nature*, 235(5334):165-166, 1972.

The virus-induced flow of phospholipids from the cytoplasmic to the nuclear membranes was investigated in the nucleocapsid of the herpesvirus in primary rabbit kidney cells. The cells were cultivated and infected with pseudorabies virus with an adsorbed multiplicity of 20 plaque-forming units/cell, then separated into fractions containing the cytoplasmic, outer nuclear, and inner nuclear membranes. Preliminary experiments were conducted to determine the distribution of labeled phospholipids among the cytoplasmic and nuclear membranes at various times after a "chase." After a 3-day chase, there was a loss of 42% of labeled phospholipid from the cytoplasmic fraction and an approximate doubling in the inner nuclear fraction. The virus-induced increase in the amount of labeled phospholipids associated with the inner nuclear membrane suggests that infection stimulates the synthesis of nuclear membrane. To ascertain that the nuclear membrane fraction obtained from infected cells was not contaminated with cytoplasmic membranes, the ratio of label in sphingomyelin to label in phosphatidylcholine in the nuclear membranes of infected and uninfected cells was determined. Since this ratio did not change, it is clear that this fraction was not contaminated. The results showed an extensive *de novo* assembly of nuclear membrane in pseudorabies virus infected cells. The virus probably buds from the newly synthesized regions. (18 refs.) - *A. C. Schenker.*

Albert Einstein Medical Center
Philadelphia, Pennsylvania 19141

1964 **WHITE, J. M.; & HARVEY, D. R.** Defective synthesis of alpha and beta globin chains in lead poisoning. *Nature*, 236(5341):71-73, 1972.

The synthesis and assembly of alpha and beta globin chains were studied in reticulocyte-rich blood samples from 3-year-old twins who developed lead poisoning after eating old paint. The cells were prepared and incubated for 60 min with $_3$H-leucine and divided into two equal aliquots. The globin designated "impure" was prepared by adding the cells directly to acid acetone, and the "pure" globin was prepared by separating the hemoglobin from other proteins by chromatography of a lysate of washed cells on G-100 sephadex. The radioactivity and absorbance of the protein fractions of the lysate eluted from the column were measured. The pure hemoglobin fraction was then concentrated by ultrafiltration and the globin precipitated by addition of acetone. The alpha and beta chains from both pure and impure globins were separated by chromatography and the radioactivity measured. The synthesis of alpha and beta chains of the reticulocytes was measured in vitro at the initial state, at 6 and 12 weeks after the onset of the illness, and after treatment with penicillamine. The hemoglobin levels were 7.0 and 7.6 gm/100ml at first stage and lead level 98 microgm/100ml. A gamma peak, associated with radioactivity patterns of alpha and beta pure and impure globins, is followed throughout the illness, and as the hemoglobin rises the alpha:beta + gamma ratio approaches 1.0. Globin synthesis is disordered in the reticulocytes of the patients. (12 refs.) - *A. C. Schenker.*

Royal Postgraduate Medical School
London, England

1965 **LEE, J. A.** Lead pollution from a factory manufacturing anti-knock compounds. *Nature*, 238(5360):165-166, 1972.

Significant levels of lead, found in vegetation close to a factory manufacturing anti-knock compounds containing tetraetheyl and tetramethyl lead, are reported in a study on edaphic factors affecting communities in Cheshire, England. Moss species from a woodland near the factory were collected and their mean lead content was taken as a measure of the lead accumulated in the ground layer. The field layer was sampled by excising green, healthy leaf blades of Holcus lanatus, and soil samples were taken from the top 2 cm of soil under tussocks of Holcus lanatus. An acetic acid soluble soil extract was prepared and lead determinations were conducted by atomic absorption flame photometry. A sample of Holcus lanatus from immediately outside the factory had a lead content of 1,838 ppm. There was a rapid decline in lead concentration in the vegetation away from the factory in the first 400m and a lower decline in the next 400m. At 800m, the amount of lead in the mosses was 2-3 times that in the same species collected from rural areas remote from industry. Levels of extractable lead in the soil were low but showed a similar pattern to that in the vegetation. (9 refs.) - *A. C. Schenker.*

University of Manchester
Manchester, England

1966 **POSWILLO, D. E.; SOPHER, DINAH; & MITCHELL, SANDRA.** Experimental induction of foetal malformation with "blighted" potato: a preliminary report. *Nature*, 239(5373):462-464, 1972.

The effect of "blighted" potato concentrate on the morphogenesis of the mammalian embryo was studied in Colworth Wistar rats and in Callithrix jacchus primates. Potatoes (Kerr's pink) were infected with Phytophtera infestans and an homogenized concentrate was prepared. The rats, divided into 3 groups of 6, 4, and 3 animals, received a daily dietary mixture of: 10 gm crushed freeze-dried "blighted" potato concentrate mixed with 10 gm Complan (Group 1); 10 gm potato starch mixed with 10 gm Complan (Group 2); and 20 gm crushed MRC b pellet diet (Group 3). The diets were commenced 2 days before mating. At day 20, after hysterectomy, embryos were examined. The potato concentrate was also administered to 6 conjugal pairs of primates; 6 female marmosets served as controls, over a 48-day period, and hysterectomy was performed shortly thereafter. The rats fed "blighted" potato concentrate showed no embryolethality or teratogenicity. Examination of the 11 fetuses in the control group of marmosets showed no abnormalities, but in the experimental group, 4 of the 11 fetuses showed cranial osseous defects on macroscopic examination. The severity of the defect appeared to be related to the length of preconception exposure of the conjugal pair to the experimental diet. A causal relationship between compounds found in "blighted" potato and cranial osseous defects is postulated. (7 refs.) - *A. C. Schenker.*

Royal College of Surgeons of England
Lincoln's Inn Fields
London WC2, England

1967 **HOLLAND, PAUL V.; ALTER, HARVEY J.; & SMITH, HOLLY M.** Technics of HAA detection. *New England Journal of Medicine*, 286(3):158-159, 1972.

The postulate by Rigoli et al. that the saline dilution method contributes to disintegration of the immunologic complex between the Australia antigen (Au, HAA) and its antibody (anti-Au, anti-HAA) is questioned. False positive tests for Au and anti-Au may occur when a triple-well rather than a double-well pattern for crossover electrophoresis (CEP) is used. There is no evidence in the literature that saline dilution alone would result in disintegration of the immunologic complex. It is submitted that Au and anti-Au are best investigated individually with a double-well CEP pattern. Furthermore, up to 0.4% humans have antibody to bovine serum constituents; if bovine thrombin is used to convert Au+ plasma to serum for reagent use, antibody to the thrombin will precipitate in CEP causing a positive reaction for anti-Au. - *A. C. Schenker.*

National Institutes of Health
Bethesda, Maryland

1968 **THALER, M. M.** Mitochondria in Reye's syndrome. *New England Journal of Medicine*, 286(8):434, 1972. (Letter)

Disagreement is voiced with the interpretation by Partin et al. of the appearance of the mitochondria as the lesion which may be instrumental in the development of Reye's syndrome. Swollen mitochondria were observed by the authors in both recovering as well as dying patients; second biopsies were not obtained in the dying, so that a conclusion that persistent mitochondrial swelling is associated with a fatal outcome is not warranted. In contrast to these findings, work is cited where mitochondrial changes were heterogeneous and relatively minor in subsequently surviving and in preterminal patients. Other investigators report that rapid conformational changes can be induced on isolated mitochondria, including swelling, by changing the concentration of energy substrates or cations, without affecting the functional integrity of the organelle. Reversible swelling of hepatic mitochondria may occur in a number of nonfatal conditions. (11 refs.) - *A. C. Schenker.*

University of California School of Medicine
San Francisco, California

1969 **PARTIN, JOHN C.; SCHUBERT, WILLIAM K.; & PARTIN, JACQUELINE S.** Mitochondria in Reye's syndrome. *New England Journal of Medicine*, 286(8):434, 1972. (Letter)

A reply is offered to Thaler's letter pointing out faulty interpretation of the mitochondrial role in Reye's syndrome. Clinically, biochemically, and ultrastructurally, the hepatic injury in Reye's syndrome is measured in hours rather than days,

and samples described in the original publication were obtained early in the syndrome; Thaler's observations were made on the twentieth day after central nervous system symptoms. The mitochondria in the surviving patients were nearly normal by the fifth or sixth day in the study originally described. The rapid conformational changes referred to (according to Hackenbrook) represent low-amplitude optical density changes which are reversible and high-amplitude optical density changes which are irreversible; these latter are similar to the irreversible changes described in the original study. (4 refs.) - *A. C. Schenker.*

Children's Hospital
Research Foundation
Cincinnati, Ohio

1970 **WILLIAMS, EIRIAN.** Lead poisoning in rural Wales. *British Medical Journal*, 3(5819):174, 1972. (Letter)

A farmer and his wife were clearly the victims of severe lead poisoning caused by the conveyance of water to the farm house through lead pipes from a remote well. The farmer was hospitalized initially with abdominal pain, anemia, and a gastric ulcer, while his wife's first complaints dealt with recurring abdominal pain and constipation, headache, backache, nervousness, and fatigue. Lead poisoning was diagnosed only subsequently, after the farmer was again admitted with colicky abdominal pain and vomiting accompanied by raised blood urea. The cause of their early symptoms was not determined, although lead may have played a part. - *B. J. Grylack.*

Pembroke County War Memorial
Hospital
Haverfordwest, South Wales

1971 **THOMAS, W.R.G.** Australia antigen in transfusions of fresh blood. *British Medical Journal*, 3(5819):173, 1972. (Letter)

Tests to detect the presence of Australia antigen were added recently to the range of posttransfusion checks made on fresh blood to be administered to patients. One Australia-antigen positive donation was discovered, and since then all fresh blood for transfusion is being checked for the presence of the antigen during cross matching. The latex agglutination test described by Leach and Ruck (1971) is quick, simple, and very sensitive and has proved to be the most suitable screen test. Dilutions of the donor serum are tested later by more specific methods such as cross-over electrophoresis and gel-diffusion methods enabling the nature of the antigen to be demonstrated by a reaction of identity. A complement fixation test, the most sensitive test for the presence of antigen, presents problems for routine use due to the scarcity of human antisera and the number of antigen positive sera which show anticomplementary activity. (3 refs.) - *B. J. Grylack.*

Group Laboratories
Mayday Hospital
Thornton Heath, Croydon, England

1972 **MACGILLIVRAY, IAN.** Treatment of severe toxaemia of pregnancy. *Lancet*, 1(7743):198, 1972. (Letter)

Successful experience with management of severe toxemia in pregnancy suggests that dialysis treatment may be unnecessary. Eight primigravidae with severe hypertensive disease of pregnancy with heavy proteinuria between 27 and 32 weeks of pregnancy were treated with sodium amylobarbitone or chlormethiazole for sedation and, when labor was induced, with 'Puroverine' and intravenous chlormethiazole. The babies were small for dates, but all survived. While the heparin used in the hemodialysis in a previous study may have been beneficial, it is unlikely that heparin can remove or dispel the fibrin already deposited in the placenta in severe preeclampsia. Heparin therapy is indicated only for incipient preeclampsia before there is any significant deposition of fibrin. - *B. J. Grylack.*

University of Aberdeen
Foresterhill, Aberdeen AB9 2ZD,
Scotland

1973 **STERN, LEO.** Drug interactions—Part II. Drugs, the newborn infant, and the binding of bilirubin to albumin. *Pediatrics*, 49(6):916-917, 1972.

In view of the fact that the production of kernicterus involves the increase of free, unbound, unconjugated bilirubin in plasma, either by dissociation from its albumin binding sites or by the introduction of 1 or more anions which compete preferentially for common or shared site, the physician administering drugs to newborn infants should resist the temptation to try a new agent with a slightly different structure unless its precise

status with respect to bilirubin-albumin binding is known. The clinical risk of free bilirubin from any drug depends upon the drug concentration itself, whether it is totally or partially competitive for binding, the *in vivo* bilirubin/albumin ratio, the simultaneous existence of other local conditions, and the presence or absence of other competitive anions. Any drug used in the newborn must be subjected to study to determine its capacity to displace bilirubin from albumin. This information is mandatory not only for related compounds but also for any formulary changes made in the drug itself. (11 refs.) - *B. J. Grylack.*

Montreal Children's Hospital
Montreal, Quebec, Canada

1974 **MAURER, HAROLD M.; & CAUL, JOYCE.** Influence of bilirubin on human platelets. *Pediatrics Research*, 6(2):136-144, 1972.

Bilirubin-induced platelet aggregation was studied *in vitro* spectrophotometrically, using a platelet aggregometer, to determine the effect of bilirubin on platelet adenine nucleotide content and its role in producing intravascular thrombosis or hemorrhage. Venous blood was collected from healthy volunteers, platelet rich plasma was collected, and studies were performed on washed platelet suspensions. Solutions of bilirubin, bilirubin-albumin mixtures, albumin, and photooxidized bilirubin were added either to washed platelet suspension mixed with 0.154 M potassium chloride and 0.11 M calcium chloride or to citrated platelet-rich plasma, and changes in light transmission were recorded. Platelet-rich plasma was also examined under the light microscope before and after treatment with solutions of bilirubin and albumin. The results revealed that washed platelets were extensively aggregated and stained with bilirubin (at concentration of 0.5 mg/100ml) whereas platelet-rich plasma revealed only weak aggregation and this only at bilirubin levels of 10mg/100ml or higher. The most rapid and extensive aggregation was found when the suspension of platelets was supplemented with both calcium and potassium. In the presence of bilirubin, adenosine diphosphate (ADP) and adenosine triphosphate (ATP) were released from the platelets. Bilirubin bound to albumin at a molar ratio of 0.75 had no effect on platelet content of these nucleotides. It is suggested that bilirubin influences platelet function. (39 refs.) - *A. C. Schenker.*

Medical College of Virginia
Virginia Commonwealth University
Richmond, Virginia 23219

1975 **THALER, M. MICHAEL; GEMES, DAVID L.; & BAKKEN, ARNE F.** Enzymatic conversion of heme to bilirubin in normal and starved fetuses and newborn rats. *Pediatrics Research*, 6(3):197-201, 1972.

The development of heme oxygenase in fetal and newborn rat liver and spleen, the effects of starvation and refeeding on heme oxygenase activity in newborns, and the influence of maternal starvation on heme oxygenase in offspring before and after birth are reported. The Ss were Sprague-Dawley rats. For microsomal heme oxygenase, a Gilford Model 2000 spectrophotometer was used. Hepatic heme oxygenase was highly active on the fifteenth day of gestation; a rapid increase occurred during the first postnatal day (0.237) increasing to a maximum at 7 days of age; activity declined subsequently to basal values at weaning. The splenic and hepatic enzyme activities follow dissimilar developmental patterns. Fasting of pregnant rats was associated with significantly increased ($p<0.05$) hepatic heme oxygenase activities in fetuses and newborn offspring. In fasting newborn rats, hepatic heme oxygenase activity increased 50% in 3 hr and doubled within 6 hr when compared with fed controls. The increase in activity during fasting and the decrease following dietary reconstitution were statistically significant ($p<0.005$). The activity of the splenic enzyme was unchanged under these conditions. The results show that the liver has a higher capacity for enzymatic conversion of heme to bilirubin in fetal and newborn rats, and that bilirubin production in the newborn is enhanced by maternal starvation or fasting of offspring after birth. (22 refs.) - *A. C. Schenker.*

University of California
(Pediatrics)
San Francisco, California 94122

1976 Case records of the Massachusetts General Hospital. *New England Journal of Medicine*, 286(5):255-260, 1972.

In the weekly clinicopathological exercises conducted at the Massachusetts General Hospital, the case of a 13-month-old boy with marked jaundice and with a clinical diagnosis of viral hepatitis was presented for consideration. The child died on the seventh hospital day when the

blood pressure rose to 190/110; the pupils were fixed and unequal (larger on the left side); and decerebrate posturing and gross hematuria were observed. Dexamethasone and mannitol treatment were of no avail. Upon consideration of the autopsy results, several events in the recent past of the child were brought out: the backing up of sewage into the family's bathtub; an injection of live measles vaccine one month before hospital admission; and no exposure to any person with hepatitis. The diagnosis of Reye's disease is ruled out by a normal glucose level (95mg/100ml). The ammonia level (150 microgm/100ml) confirms the impression that the probable cause of neurologic signs was hepatic coma. The exchange transfusion, used in a moribund state, was of no avail. The postmortem diagnosis was fulminant hepatic failure secondary to viral hepatitis and gram-negative sepsis and disseminated intravascular coagulation. The pathological findings were: capsular wrinkling, condensation of the vascular structures and a nutmeg parenchymal pattern, collapsed lobules containing proliferated bile ductules, and replacement of the hepatic cell cords by necrotic debris. (17 refs.) - *A. C. Schenker.*

1977 **GERCKEN, G.; TILING, T.; BROCKMANN, U.; & SCHROTER, W.** Fatty acid composition of phospholipids in erythrocytes of adults, normal newborn infants, and neonates with Rh erythroblastosis. *Pediatrics Research*, 6(3):487-494, 1972.

The deviating total phospholipids (PL) and fatty acid compositions of erythrocytes of newborn infants were compared with those of erythrocytes from adults and neonates with Rh erythroblastosis to determine whether these patterns were associated with shortened life span, great sensitivity toward oxidative drugs, or changed permeability and decreased mechanical resistance of these cells. Venous blood was obtained from each of 5 healthy adults (22-35 years) and cord blood was obtained from 5 normal neonates and from 4 neonates with Rh erythroblastosis. Erythrocytes were isolated by centrifugation, washed, and resuspended. Extraction of lipids was carried out by a modified procedure of Ways and Hanahan. PL in the lipid extract were separated from glycolipids and neutral lipids by thin-layer chromatography (TLC) and further analysis was performed by gas-liquid chromatography (GLC). The pattern of fatty acids in erythrocytes of newborn infants differed significantly from that in erythrocytes of adults: although the proportion of unsaturated fatty acids was smaller in erythrocytes from neonates than in those from adults, the proportion of polyunsaturated fatty acids was greater; within the oleate and linoleate family there was a shift toward more highly unsaturated fatty acids. The fatty acid pattern in the erythrocytes of the neonates resembled that of a deficiency of essential fatty acids; neonates with Rh erythroblastosis revealed a normal pattern for newborn infants. (51 refs.) - *A. C. Schenker.*

University of Hamburg
Papendamm 6, Germany

1978 **NORMAN, A. P.; HARVEY, D. R.; KOVAR, ILYA; & CAMPBELL, NEIL.** Oxytocic agents and neonatal hyperbilirubinaemia. *Lancet*, 2(7784):972, 1972. (Letter)

In the light of a striking increase in hyperbilirubinemia in full-term and other newborn infants, the link between this increase and the increased use of oxytocin and accelerated labor is being probed. At present, the evidence is far from being conclusive, but no other obvious fetal or maternal factor has been found that can be implicated. (2 refs.) - *B. J. Grylack.*

Queen Charlotte's Maternity
Hospital
London W.6, England

1979 **PURVIS-SMITH, S. G.; HAYES, KATHLEEN; & MENSER, MARGARET A.** Dermatoglyphics in children with prenatal cytomegalovirus infection. *Lancet*, 2(7784):976-977, 1972. (Letter)

Dermatoglyphics were reported for 11 congenital cytomegalovirus (CMV) children (6 males), their parents, and 1 sibling from each of 6 families (5 males). Patients' ages ranged from 2 months to 4 years. The dermatoglyphics of the affected children showed a raised frequency of digital whorl patterns, and it was suggested that the incidence of unusual palmar creases might also be increased. The incidence of digital whorls in the fathers of the CMV patients in this and a similar study was higher than that in the patients or in normal controls. Patients with congenital rubella, congenital CMV, and acute childhood leukemia have raised digital whorl frequencies and their fathers have whorl frequencies that are considerably higher than in male controls. It is possible that

genetic factors controlling immune responses are inherited from the father and predispose a particular fetus to these disorders. (13 refs.) - *B. J. Grylack.*

Royal Alexandra Hospital for
Children
Camperdown, N.S.W. 2050
Australia

1980 **COMMITTEE ON ENVIRONMENTAL HAZARDS.** Lead content of paint applied to surfaces accessible to young children. *Pediatrics*, 49(6):918-921, 1972.

The American Academy of Pediatrics endorses the principle contained in the petition filed with the Commissioner of the Food and Drug Administration that paints containing more than minute traces of lead be declared as banned, hazardous substances. To preserve health and prevent adverse metabolic effects, the total daily intake of lead should be limited to <300μg Pb. The prevalence of pica in young children is significant, an estimated 50% of children between ages 1 and 3 years repetitively ingesting nonfood substances. Not only should the present American National Standards Institute standard be reduced to <0.06%, but a similar Federal standard should be instituted in order to minimize lead as a health hazard to future generations of children. (6 refs.) - *B. J. Grylack.*

1981 **PIOMELLI, SERGIO; DAVIDOW, BERNARD; GUINEE, VINCENT F.; YOUNG, PATRICIA; & GAY, GISELLE.** The FEP (free erythrocyte porphyrins) test: a screening micromethod for lead poisoning. *Pediatrics*, 51(2):254-259, 1973.

The correlation between the results of the free erythrocyte porphyrins (FEP) test and the whole blood lead (Pb) levels was evaluated. The FEP test on 20 microliters of blood, which combines a simplified extraction procedure with the use of fluorometry and is known to parallel lead concentration in severe lead intoxication, was compared with blood lead levels according to a modification of the Hessel method. Samples of known blood Pb level were selected among the samples tested by the New York City Department of Health Bureau; FEP concentration was evaluated in 1038 of these. There was a good correlation in blood samples with Pb levels of 40 microgm/100ml or higher, between the FEP and blood Pb levels; the coefficient of correlation was .72 ($p<0.001$). The FEP test detects the interference of lead with heme synthesis in the bone marrow, a direct effect of toxicity. The observations indicate that the FEP test could be of great advantage as a screening test for high risk individuals in terms of lead intoxication. (18 refs.) - *A. C. Schenker.*

New York University Medical
Center
New York, New York 10016

1982 **PAPAEVANGELOU, GEORGE J.** Hepatitis B in infants. *New England Journal of Medicine*, 288(18):972, 1973. (Letter)

The hypothesis that transmission of hepatitis B antigen (HB Ag) from mother to infant at the time of birth is the basis for both the acquisition and the persistence of HB Ag in asymptomatic carriers, as postulated by Merrill, is untenable. The cases of overt viral hepatitis B among pregnant women are not significantly common to explain the high frequency of asymptomatic carriers in some parts of the world. Among 295 pregnant women, 11 asymptomatic HB-Ag carriers were detected and these mothers and their infants were followed for 67-700 days. The infants were examined at 3-month intervals and all remained clinically well. However, HB Ag was detected in 2 cases, one when the infant was 6 months old and the other when he was 14 months old, both remaining well. When tested 3 and 6 months later, their blood did not contain HB Ag. In contrast to infants born to mothers with overt acute hepatitis B, these infants were capable of eliminating the AB Ag. (3 refs.) - *A. C. Schenker.*

University of Athens School of
Medicine
Athens, Greece

1983 **MERRILL, DEBORAH A.; DUBOIS, REUBEN S.; & KOHLER, PETER F.** Hepatitis B in infants. *New England Journal of Medicine*, 288(18):973, 1973. (Letter)

In reply to comments on the article concerning hepatitis B in infants, agreement is voiced with McGill and Taswell's opinion that hepatitis B antigen (HB Ag) can be transmitted from asymptomatic maternal carriers to their infants as well as from acutely ill HB-Ag positive mothers. The

presence of both HB Ag and HB Ab in the carrier mother, described by McGill and Taswell, is of interest and it is suggested that if the infant's serum was negative for HB Ab by hemagglutination, perhaps the maternal HB Ab is IgM. In answer to Dr. Papaevangelou's comments, it was not meant to imply that neonatal acquisition of HB Ag occurs frequently enough to account for the high carrier rate in certain adult populations; predisposing genetic factors cannot be excluded as a cause of the asymptomatic carrier state, as Dr. Papaevangelou suggests. - *A. C. Schenker.*

University of Colorado Medical
Center
Denver, Colorado

1984 **MCGILL, DOUGLAS B.; & TASWELL, HOWARD F.** Hepatitis B in infants. *New England Journal of Medicine*, 288(18):972-973, 1973. (Letter)

In reference to Merrill's article on 4 carrier infants of hepatitis, an additional mother-infant pair is described wherein the mother was a carrier. The mother had been antigen-positive and clinically characterized as having chronic persistent hepatitis. Although her baby was negative at birth and at 6 weeks, at 3 months the infant was strongly antigen-positive on counterelectrophoresis. At the time of birth the umbilical cord blood was negative on counterelectrophoresis but positive by radioimmunoassay. The infant is now clinically well. The father's serum was strongly positive by modified agar-gel diffusion, although he has displayed no symptoms of hepatitis. No antibody was detected in the serum of either mother or infant by any of the above techniques. However, the mother's serum was positive for antibody by hemagglutination, and when concentrated, by agar-gel diffusion. Additional mother-infant pairs need to be studied by the more sensitive methods before it can be concluded that transmission by an extrauterine route is a common occurrence. (2 refs.) - *A. C. Schenker.*

Mayo Clinic
Rochester, Minnesota

1985 **KATZ, J.; & MARCUS, R. G.** The risk of Rh isoimmunization in ruptured tubal pregnancy. *British Medical Journal*, 3(5828):667-669, 1972.

Investigation of 38 African women hospitalized with ruptured tubal pregnancies revealed a fetal cell score of 5 or more per 15,000 in 4 out of 20 preoperative venous samples and in 9 out of 38 postoperative venous samples, patients with the highest intraperitoneal counts showing the greatest numbers of fetal cells in the maternal circulation ($r=0.03146$, $p<0.001$). In 40 nonpregnant African women the maximum number of stained cells resembling fetal cells detected in the blood by the acid elution technique was 2 per 150,000 erythrocytes; on 5 of these Ss the fetal cell score was 1 or 2 per 150,000. The high incidence (23.7%) of significant fetomaternal hemorrhage found after a ruptured tubal pregnancy, a figure significantly higher ($p<0.02$) than that found after abortion, indicates that this may be an important source of Rh isoimmunization. The finding of fetal blood in the maternal circulation probably reflects the fact that erythrocytes introduced into the peritoneal cavity are absorbed into the systemic circulation. (23 refs.) - *B. J. Grylack.*

University of the Witwatersrand
Johannesburg, South Africa

1986 **WILLIAMS, M. K.** Lead poisoning. *British Medical Journal*, 3(5826):586-587, 1972. (Letter)

Lead poisoning among thousands of lead workers in Europe and the United States has been reported to be prevented by maintaining blood lead at less than 80 μg/100ml, yet a recent study associates blood lead below this level with symptoms and signs. The discrepancy is probably due to the tendency to diagnose lead poisoning in any individual with slightly increased lead absorption who is referred to a hospital with undiagnosed abdominal or joint pain, tremor, nervousness, or anemia. In such cases, epidemiologically acceptable evidence of a causal relationship between the symptoms and the lead absorption level is not available. (1 ref.) - *B. J. Grylack.*

Leatherhead, Surrey, England

1987 **AULD, ANDREW; & MCNICOL, EVELYN M.** Rhesus isoimmunization and twins. *British Medical Journal*, 3(5826):587, 1972. (Letter)

Rhesus isoimmunization was associated with multiple pregnancy in the case of a 30-year-old woman pregnant for the fourth time, with blood group O rhesus negative, probably genotype cde/cde. The

father was group A rhesus positive, probable genotype CDe/CDe. A diagnosis of twins was made at her visit at 29 weeks' gestation, and antibodies were found. Two premature, uniovular, male children weighing 1.65 and 1.6 kg were delivered by cesarean section at the end of the thirty-sixth week. Multiple replacement transfusions were carried out. Accurate prediction for each child and intrauterine transfusion were precluded by the position of the placentae and the sacs. (3 refs.) - *B. J. Grylack.*

Robroyston Hospital
Glasgow, Scotland

1988 **LIVERSEDGE, L. A.; LONGSON, MAURICE; & MACCALLAM, F. O.** Herpes encephalitis. *British Medical Journal*, 3(5825):527, 1972. (Letter)

An ad hoc working party of neurologists, neurosurgeons, neuropathologists, and virologists from the United Kingdom, Western Europe, and the United States has begun to study the problem of herpes encephalitis in detail and seeks the cooperation of other interested parties. The group has helped to initiate a survey of all cases of herpes encephalitis reported to the Public Health Laboratory in 1971. Reports of as many cases as possible will aid a multiple-center collaborative study of the various types of therapy for this condition. - *B. J. Grylack.*

Manchester Royal Infirmary
Manchester, England

1989 **GARDNER, P.S.; MCGUCKIN, ROSEMARY; & MCQUILLIN, JOYCE.** Adenovirus demonstrated by immunofluorescence. *British Medical Journal*, 3(5819):175, 1972. (Letter)

Although 6.5% (65 out of 1,028) of acute respiratory infections of childhood were associated with adenovirus infection, only 2% could be diagnosed by the indirect immunofluorescent technique. Fluorescent positive cells occurred most frequently in upper respiratory tract infections (18 out of 23) but rarely in croup, bronchitis, bronchiolitis, or pneumonia. Immunofluorescence appears to be uneconomical for the diagnosis of respiratory infections by this group of viruses. (4 refs.) - *B. J. Grylack.*

Royal Victoria Infirmary
Newcastle on Tyne, England

1990 **WALDRON, H. A.** Lead poisoning. *British Medical Journal*, 3(5830):827, 1972. (Letter)

Since the 1968 statement on blood lead levels, evidence has indicated that there is no threshold below which lead does not interfere with metabolism. Any recommendation concerning acceptable blood levels of any toxic agent must reflect the available evidence and should be altered, therefore, as new information is presented. (2 refs.) - *B. J. Grylack.*

1991 **MALCOLM, D.** Lead poisoning. *British Medical Journal*, 3(5836):366, 1972. (Letter)

Lead poisoning was established on the basis of a clinical diagnosis without other evidence or the exclusion of other causes in several patients with urinary α-aminolevulinic acid levels within safe limits and with coproporphyrin in urine within the normal range for people not exposed to lead. Blood lead levels were also within safe limits. The acceptable levels of coproporphyrin and of α-aminolevulinic acid in urine recognize that lead affects enzyme systems without producing symptoms. Therefore, interlaboratory trials are of great importance, especially when carrying out blood lead analysis. (3 refs.) - *B. J. Grylack.*

1992 New influenza. *British Medical Journal*, 3(5835):251-252, 1972.

The appearance of a new strain of influenza A virus (A/England/42/72) in Britain and some other countries last winter and its implication in outbreaks in the Far East and possible involvement in future outbreaks emphasize the importance of the influenza surveillance carried out by the World Health Organization and the need for further epidemiologic research. In particular, the epidemiologic significance of minor antigenic changes in those antigens of the virus associated with immunity, namely the hemagglutinin and the neuraminidase, must be determined. The use of genetic recombinants should reduce by several months the time usually required to produce the first 250,000 doses to combat the A/England/42/72 strain. (10 refs.) - *B. J. Grylack.*

1993 **DAWBER, RODNEY P.R.** Idoxuridine and erythema multiforme after herpes simplex. *British Medical Journal*, 3(5835):300, 1972. (Letter)

Five patients with recurrent herpes simplex infection associated with erythema multiforme were treated with topical 5% idoxuridine in 100% dimethylsulphoxide (a powerful solvent and keratolytic substance) to try to modify or prevent erythema multiforme. Four patients in whom the eruption appeared to be aborted developed erythema multiforme, the earliest 9 days and the latest 14 days after the onset of the herpetic sore. Each case had clinical severity similar to previous attacks. The fifth patient derived no apparent benefit from the idoxuridine. Four patients have since had further herpetic attacks and have developed erythema multiforme again, while the fifth patient has had no recurrence of herpes simplex or erythema multiforme. It appears that shortening the course of the herpetic lesion with idoxuridine has no effect on the severity or duration of the erythema multiforme, although prevention of further herpes simplex infection seemed to prevent erythema multiforme. (3 refs.) - *B. J. Grylack.*

North Staffordshire Medical Centre
Stoke-on-Trent, England

1994 **BARR, RONALD D.** Rh isoimmunization in ruptured pregnancy. *British Medical Journal*, 3(5835):295-296, 1972. (Letter)

In view of the omissions and errors in the paper by Drs. J. Katz and R. G. Marcus on the risk of Rh isoimmunization in ruptured tubal pregnancy, it is not surprising that they have discovered only 1 record of Rh isoimmunization supposedly resulting from tubal pregnancy. The authors cite as the only evidence of fetomaternal hemorrhage the demonstration of acid-resistant cells in the maternal circulation, and they dismiss the possibility that these cells might be of maternal rather than fetal origin. Moreover, since angioblastic tissue differentiates in only the third week of life and blood cells can be recognized only subsequently, it is improbable that even the total blood volume of a 6- to 10-week embryo after intraperitoneal dilution, as the authors propose, in what is often several liters of maternal blood could account for the scores given for acid-resistant cells in the intraperitoneal and maternal peripheral venous blood. Finally, the authors unfortunately omit any comment on the Rh phenotype of their patients. (4 refs.) - *B. J. Grylack.*

Department of Medicine
University of Aberdeen
Aberdeen, Scotland

1995 **MAIR, HELENE J.; & BUCHAN, ALAN R.** Rubella vaccination and termination of pregnancy. *British Medical Journal*, 3(5835):271-273, 1972.

Termination of pregnancy after rubella vaccination was considered necessary on 6 occasions between February 1970 and May 1972 in Leicestershire (England). Two women, known to be seronegative before vaccination, were advised not to become pregnant for at least 8 weeks. One started menstruation the day after vaccination but conceived with the next 14 days. Rubella vaccine was given to the other 4 women without previous estimation of their immune state. In 4 cases vaccination was carried out within a week of the first day of the last menstrual period. Administration of rubella vaccine soon after the beginning of menstruation or early in the postpartum period is, thus, no guarantee against conception occurring in the potentially dangerous period, and any woman of childbearing age who is susceptible to rubella should be offered vaccination and be informed of the possible danger and advised of an effective contraceptive method for 2 months before and 2 months following vaccination. (10 refs.) - *B. J. Grylack.*

Public Health Laboratory
Leicester, England

1996 **BECROFT, D.M.O.; & WEBSTER, D. R.** Aflatoxins and Reye's disease. *British Medical Journal*, 3(5832):117, 1972. (Letter)

Aflatoxins were sought in the tissues of a dying 22-month-old Polynesian boy whose illness was typical of Reye's syndrome and a dying 8-month-old Caucasian girl in whom the association of severe bile duct proliferation with diffuse fatty change in her liver was considered consistent with the chronic effects of such a toxin. The 4 separate extractions made of liver tissue from Case 1 and the 3 extractions of the liver of Case 2 all contained a blue fluorescing material with the same Rf as aflatoxin B_1 and, variably, a green fluorescing material with Rf corresponding to aflatoxin G_1. It was interesting but probably coincidental that Case 1 was from an immigrant family with a large daily consumption of rice and that the symptoms of Case 2 began after solid foods, including baby rice, were introduced. (10 refs.) - *B. J. Grylack.*

University of Auckland
Auckland, New Zealand

1997 Neonatal behaviour and maternal barbiturates. *British Medical Journal*, 3(5832):63-64, 1972.

Abnormal behavior was reported in 15 infants born to mothers taking barbiturates throughout pregnancy or its final trimester and in 13 infants with congenital heroin addiction, but important differences were noted. Infants of mothers taking barbiturates were fully grown and showed no respiratory depression in the perinatal period, while 5 of 6 infants of heroin addicts weighed less than 2.5kg at birth, and 6 had an Apgar score of less than 6. The onset of symptomatology was also later in the barbiturate group. Most of the infants of mothers taking barbiturates remained restless, tremulous, or febrile, and 3 of them showed poor weight gain after birth. The influence of mothering effects on these infants' symptoms should be considered, since approximately half of the mothers on barbiturates were unable to provide adequate care and attention. (12 refs.) - *B. J. Grylack.*

1998 **DE B. MITFORD-BARBERTON, G.** Rh isoimmunization from ruptured tubal pregnancy. *British Medical Journal*, 3(5833):177, 1972. (Letter)

Experience in East Africa, where ruptured ectopic pregnancies are common, with a high mortality rate, and rhesus sensitization is uncommon, indicates that many patients will die if deprived of the safeguard of autotransfusion. Regardless of the risk of rhesus isoimmunization, autotransfusion is necessary when the condition of the patient is critical. - *B. J. Grylack.*

1999 **GOLDBERG, ABE.** Lead poisoning. *British Medical Journal*, 3(5834):230, 1972. (Letter)

No rigid inflexible level of blood lead such as 80 μg/100ml can be accepted in the clinical agreement of nonindustrial patients who are exposed. A previous statement indicating that levels below this amount are associated in many cases with symptomatology was made on the basis of study of industrial lead poisoning in selected strong men who had often been on the job for many years. In contrast, a study of rural, domestic Ss dealt with a wide age group, with women and children as well as men, and with exposure to an excess of lead in the water supply. (1 ref.) - *B. J. Grylack.*

Stobhill General Hospital
Glasgow, Scotland

2000 **MCNICOL, EVELYN M.; & AULD, ANDREW.** Rhesus isoimmunization and twins. *British Medical Journal*, 3(5834):238-239, 1972. (Letter)

A second case of multiple pregnancy in association with rhesus immunization involved a 27-year-old gravida-5 found at approximately 22 weeks to have a twin pregnancy. She was group O rhesus negative, probably genotype cde/cde, and her husband was group O rhesus positive, probably genotype CDe/CDe. Ultrasound showed the placentas to be in the upper segment posteriorly and the fetuses lying side by side. Intrauterine transfusion of both fetuses was planned, but neither fetal heart could be heard after 3 days. The patient subsequently aborted hydropic twins and was later sterilized. Unlike the case reported earlier, it was hoped that accurate assessment and adequate therapy would be made possible here by the position of the sacs and placentas. - *B. J. Grylack.*

Robroyston Hospital
Glasgow, Scotland

2001 **PHILLIPS, PAUL E.** Guillain-Barre syndrome after measles. *British Medical Journal*, 3(5831):50, 1972. (Letter)

It is questionable whether the 2 cases of Guillain-Barre syndrome after measles described previously actually had either disease. Neither the clinical nor laboratory data support the diagnosis of measles beyond doubt, and the increased protein in cerebrospinal fluid without an increase in cells used to diagnose the Guillain-Barre syndrome was not reported for either patient. They probably had primarily encepahalomyelitis with a polyneuritis, which has been seen following measles and other infectious diseases. (3 refs.) - *B. J. Grylack.*

Cornell University Medical College
Hospital for Special Surgery
New York, New York

2002 **BANATVALA, J. E.; & BEST, JENNIFER M.** Rubella vaccination. *British Medical Journal*, 3(5825):525-526, 1972. (Letter)

Insufficient attention is being directed towards the development and characterization of virus strains

which may be more suitable for rubella vaccines than those currently licensed. It has become increasingly evident that local (nasopharyngeal) antibody, particularly immunoglobulin A, is important in preventing infection by viruses which gain entry through the respiratory tract. Whereas naturally acquired rubella induces local antibody, vaccines do not, with the possible exception of the RA 27/3 vaccine, especially when administered intranasally. Reports of lower incidence of congenitally acquired rubella infection in Japan as compared with western countries and of higher interferon levels in human placental cell cultures induced with Japanese than with United States and United Kingdom low-passage isolates and vaccine strains must be confirmed, but they suggest that such strains might produce satisfactory vaccine strains. (8 refs.) - *B. J. Grylack.*

St. Thomas' Hospital
London S.E.1, England

2003 **GAJDUSEK, D. C.; & GIBBS, C. J., JR.** Transmission of kuru from man to rhesus monkey (Macaca mulatta) 8½ years after inoculation. *Nature*, 240(5380):351, 1972.

The transmission of neurological disease from a human to a rhesus monkey following an incubation period of 8 years 5 months after inoculation intracerebrally and intravenously with a 10% suspension of brain tissue from a human kuru patient is described. Histopathological examination of the brain of the animal confirmed this transmission. After this prolonged interval of incubation, the animal climbed with reluctance and caution and became withdrawn and docile, with piloerection over the entire body. One and a half months after onset, the animal developed clonic jerks of all 4 limbs and trunk and almost continuous generalized tremors. The symptoms worsened, the animal having to be fed by hand whilst lying on her side; she was sacrificed at this stage of the disease. Morphological examination of the brain revealed severe status spongiosus of the cerebral cortex and basal ganglia, with marked intraneuronal vacuolation, loss of neurones, and astroglial proliferation and hypertrophy in all areas examined. This is the first case of such transmission in the old world monkey. (2 refs) - *A. C. Schenker.*

National Institute of Neurological
Diseases and Stroke
Bethesda, Maryland

2004 **BLUMBERG, B. S.; VIERUCCI, A.; LONDON, W. T.; & SUTNICK, A. I.** Association of antibodies to Australia antigen with anti-Gm antibodies in Italian patients with thalassaemia. *Nature*, 236(5340):28-30, 1972.

Based on the concept that Australia antigen is an infectious agent which causes hepatitis in man and has many of the properties of a serum protein polymorphism, 169 thalassemia patients were examined. Anti-Gm was determined by the method of Ropartz (classified mostly as anti-Gm(1); the immunodiffusion method of Blumberg and Riddell was used for Au(1) and anti-Au(1) determinations. There were 30 patients with anti-Au(1) a of which 22 also had anti-Gm, a significantly higher frequency than anti-Gm patients who had persistent Au(1) in their blood ($P = 0.0088$). It is also significantly greater than the frequency of anti-Gm patients who have neither Au(1) nor anti-Au(1) ($P = 0.0203$). These results led to the hypothesis that if Australia antigen has the properties of a polymorphism and contains the Gm groups, antibody formation to both Gm and Qu(1) would be more common in patients who lack Gm phenotypes. This hypothesis was consistent with the finding that the frequency of Gm types was always greater in thalassemia patients who had developed persistent Australia antigen than in those who had developed anti-Au(1). (9 refs.) - *A. C. Schenker.*

Institute for Cancer Research
Philadelphia, Pennsylvania

2005 **EYLAR, E. H.; JACKSON, J.; ROTHENBERG, B.; & BROSTOFF, S. W.** Suppression of the immune response: reversal of the disease state with antigen in allergic encephalomyelitis. *Nature*, 236(5441): 74-76, 1972.

The effect of antigen on allergic encephalomyelitis (EAE) experimentally produced in rhesus monkeys by means of human Al protein was studied. EAE was induced by intradermal injections of a total of 5mg of a homogeneous preparation of human A1 protein. Sensitized animals were observed for clinical signs (anorexia, ptosis of eyelids, tremors, lethargy, loss of coordination, leg weakness, or paralysis) which developed 13-26 days after sensitization. Suppressive treatment was initiated by i.m. injection of human protein (about 10mg); 2-hydroxy-5-

nitrobenzyl bromide (HNB)-modified A1 protein with blocked tryptophan residue was also used for suppressive treatment. Therapeutic injections were given within 24-48hr after signs of EAE; after the first injection, 2-3mg antigen was given daily for at least 12 days. The results showed that only 3 of the 16 animals treated with either A1 protein or HNB-A1 protein died, whereas all control animals died. Of the surviving animals, 8 were examined for humoral antibody; 3 animals had antibody titres of 1/64-1/512 at 1-2 weeks after the last injection for suppression. The clinical signs in all 13 surviving monkeys had disappeared after 7 days. The study appears to be one of the first cases of complete reversal of an experimentally produced autoimmune disease after manifestation of definite clinical signs (38 refs.) - *A. C. Schenker.*

The Merck Institute
Rahway, New Jersey 07065

2006 **MIZUTANI, HIROMICHI.** Skin-test reactions in patients with SSPE. *New England Journal of Medicine*, 286(1):48, 1972. (Letter)

Negative reactions to skin tests with a measles vaccine, reported by Gerson and Haslam in several cases of subacute sclerosing panencephalitis (SSPE), are discussed. It is suggested that the live measles-virus vaccine used by Gerson and Haslam as an antigen contains antibiotics and a stabilizer and therefore lacks specificity. The study by these authors is criticized on the grounds that it lacks healthy controls with previous histories of rubeola who might also have reacted negatively on skin tests. There is also a question, based on the cited study, as to whether the tests were performed with the patients in a stage of generally diminished cellular immunity. (3 refs.) - *A. C. Schenker.*

Kanto Teishin Hospital
Tokyo, Japan

2007 **GERSON, KENNETH L.; & HASLAM, ROBERT H. A.** Skin-test reactions in patients with SSPE. *New England Journal of Medicine*, 286(1):48, 1972. (Letter)

A reply is offered to the criticisms presented by Mizutani with respect to a study on immunologic abnormalities occurring in cases of subacute sclerosing panencephalitis (SSPE). Mizutani's results with the measles antigen which he describes leave some doubt as to whether this skin test demonstrates cellular immunity. Normal children with measles antecedents have strong inhibition of leukocyte migration with the same antigen. The contention that patients with SSPE demonstrate a functional defect in thymus derived lymphocyte population is based on the response to Candida albicans and streptokinase-streptodornase, failure to reject skin grafts in the usual time, and failure of contact sensitivity to dinitrochlorobenzene to develop. (2 refs.) - *A. C. Schenker.*

University of Kentucky
Medical Center
Lexington, Kentucky

2008 **LIN-FU, JANE S.** Undue absorption of lead among children -- a new look at an old problem. *New England Journal of Medicine*, 286(13):702-710, 1972.

A daily intake of 1-2mg of lead for 5-6 mos has been shown to be sufficient to cause symptomatic poisoning in 2-year-old children. Although a blood level of lead below 60 microgm/100 gm is seldom encountered in overt symptoms of lead poisoning in children, a number of studies have shown that this level is too high to be accepted as the upper limit of normal. In Chicago and New York City, 20% or more of the children between ages 1 and 6 years had blood lead values of over 40 microgram/100 ml; the fact that normal lead values for children have indicated higher values than those of adults is probably due to the fact that the child studies were mostly from urban areas. Early recognition of undue lead absorption among children is important for the prevention of lead poisoning; such absorption may promote deleterious subclinical effects, and young children may be particularly vulnerable to the toxic effects of lead. In man, the inhibitory effect of lead on delta-amino-levulinic acid dehydrase (ALA-D) has been confined to erythrocytes of peripheral blood, but in laboratory animals this effect has been demonstrated in brain, liver, kidneys, and bone marrow. (83 refs.) - *A. C. Schenker.*

Mental and Child Health Service
Room 12-07 Parklawn Bldg.
5600 Fishers Lane
Rockville, Maryland 20852

2009 **CONNOR, JAMES D.; & NYHAN, WILLIAM L.** Haemophilus influenzae infections. *New England Journal of Medicine*, 286(2):107, 1972. (Letter)

With reference to the 40% increase of admissions (over the past 25 years) for influenzal meningitis to the Children's Hospital in Pittsburgh reported by Michaels, it is submitted that such increase is not universal throughout the United States. In Jackson Memorial Hospital in Miami, there was a slight decrease in such cases from 1959-1966. During this period the total number of pediatric admissions nearly doubled, and the annual total number of serious infections due to *Haemophilus influenzae (H. influenzae)* remained about the same. There was an unusual number of infections due to *H. influenzae* in the very young. A shift in protection of newborn infants may be the reason for this, and such shift may be modulated by environment, accounting for the differences in the incidence of the disease. (5 refs.) - *A. C. Schenker.*

University of California
School of Medicine
San Diego, California

2010 **MICHAELS, RICHARD H.** Haemophilus influenzae infections. *New England Journal of Medicine*, 286(2):107-108, 1972. (Letter)

A reply is offered on the subject of differences in incidence of Haemophilus influenzae *(H. influenzae)* between Pittsburgh and Miami, as presented by Connor and Nyhan. In Pittsburgh, the increase in *H. influenzae* is not due to greater numbers of very young infants with infections due to *H. influenzae* excluding meningitis. The youngest child with epiglottitis was 5 mos of age, and only one of the 36 children with other bacteremic infections was less than 3 mos old. Infants under 3 mos of age still account for a small proportion of the total number of Pittsburgh cases, consistently 3-4% during the past 3 decades. - *A. C. Schenker.*

Children's Hospital of Pittsburgh
Pittsburgh, Pennsylvania

2011 **GINSBERG, ALLEN L.; *CONRAD, MARCEL E.; BANCROFT, WILLIAM H.; LING, CHUNG M.; & OVERBY, LACY R.** Prevention of endemic HAA-positive hepatitis with gamma globulin: use of a simple radioimmune assay to detect HAA. *New England Journal of Medicine*, 286(11):562-566, 1972.

A simple radioimmune assay method (RIA) to detect Australia (HAA) antigen in serum was developed to test Ss among both normal blood donors and patients with hepatitis. Normal Ss were 1,133 recruits at Fort Dix who were found to be suitable as blood donors; patients with hepatitis were 211 American soldiers stationed in Korea; only icteric cases of hepatitis were included in the study. Hepatitis was confirmed by liver biopsy specimens. Patients with hepatitis were admitted to the hospital from a large population of soldiers who had received either 2ml, 5ml, or 10ml of human serum gamma globulin, or a 2.5% albumin solution in potassium glutamate. Serum from all Ss was coded and tested for HAA by various known methods; the RIA was performed with the use of guinea-pig anti-HAA labeled with ^{125}I. Among the 1,133 serum specimens from blood donors, 3 were found HAA-positive by a complement fixation (CF) method; the same 3 and 7 additional specimens were positive by RIA. Among the specimens from patients, 25% were HAA-positive by RIA, whereas 12.8%, 11.8%, 9%, and 4.7% were found positive by 4 other methods. There was a poor correlation between the CF titer and the amount of radioactivity found by RIA. The protective effect of gamma globulin in HAA-negative hepatitis was similar to that observed in other studies. The RIA method of detection of HAA is highly sensitive. (26 refs.) - *A. C. Schenker.*

*Walter Reed Army Institute
of Research
Washington, D.C. 20012

2012 **ALTER, J. J.; HOLLAND, P. V.; SCHMIDT, P. J.; & PLOTZ, P. H.** Gamma-globulin for hepatitis-virus B. Prevention or extension. *Lancet*, 1(7760):1110-1111.

Until more adequate controlled trials are conducted, the posited protective role of γ-globulin against hepatitis B should not be accepted as proved. To date the available evidence indicates that immune serum globulin (ISG) attenuates but does not prevent either hepatitis A or B. Specifically in the case of hepatitis B, therefore, it must be considered whether attenuation will only increase the frequency of the carrier state, trading decreases in acute morbidity and mortality for increases in the number of persistent carriers, in chronic morbidity, and in long-term fatality. At the very least there is sufficient evidence from recent studies to indicate that this might be the case and, therefore, to warrant caution in acting

on something of such long-range importance to both patient and community. (20 refs.) - *N. Mize.*

National Institutes of Health
Bethesda, Md. 20014

2013 **KUSHNICK, THEODORE.** Why a damaged baby? *Clinical Pediatrics*, 11(4):250, 1972.

In 1955 the virus which causes cytomegalic inclusion disease was successfully isolated for the first time. The discovery occurred because the multiple symptoms of a baby girl—including neonatal hepatitis of undetermined etiology, microcephaly, ependymal calcification, and splenomegaly—went beyond the limits of existing diagnostic knowledge, causing a bewildered examining physician to send a section of the liver biopsy to a special laboratory for an attempt at viral isolation. The cytomegalic inclusion disease diagnosis is now commonplace, but the history of its initial identification should alert present-day physicians to the need for thoroughly recording all observations, even though the actual significance of such findings may only be apparent in the future. (1 ref.) - *N. Mize.*

New Jersey College of Medicine and Dentistry
Newark, N.J.

2014 **FISER, ROBERT H.; KAPLAN, JOSEPH; & HOLDER, JOHN G.** Congenital syphilis mimicking the battered child syndrome. *Clinical Pediatrics*, 11(5):305-307, 1972.

A case of congenital syphilis in a 5-week-old black girl, originally misdiagnosed as exhibiting the battered child syndrome, emphasizes the importance of obtaining serologic testing throughout pregnancy. Early in gestation a test for syphilis in the mother had been negative. This test result, coupled with a family history suggestive of an unstable home environment, led examining physicians to enter the battered child diagnosis when the infant was hospitalized for a lack of movement in both arms. Further x-ray studies uncovered multiple bone lesions compatible with a diagnosis of congenital syphilis. Subsequent serologic tests in both mother and child confirmed this relatively infrequent diagnosis. (7 refs.) - *N. Mize.*

USAMRIID
Frederick, Md. 21701

2015 **SISSON, THOMAS R. C.** The placental transfusion. *Clinical Pediatrics*, 11(5):251-252, 1972.

Controversy surrounding the value of placental transfusion in the newborn, actually a transfer of an excess of blood to the infant, continues unabated. Considering all the evidence, pro and con, it seems relatively safe to suggest that for a full-term infant, a moderate placental transfusion—resulting in the normal course of delivery from a combination of gravity, the length of time before clamping, stripping of the cord toward the infant, and the onset of respiration—is beneficial. This is especially true for infants delivered by cesarean section in whom an additional blood loss may further compromise the newborn's status. In consideration of the known disadvantages, however, disadvantages associated with hyperbilirubinemia, abnormally high venous pressures, and respiratory distress, placental transfusion may be harmful in the premature infant who typically shows less resilience in accommodating to an increased blood volume. (12 refs.) - *N. Mize.*

Temple University School of Medicine
Philadelphia, Pa. 19140

2016 **SCANLON, JOHN.** Early recognition of neonatal sepsis. *Clinical Pediatrics*, 11(5):258-260, 1972.

Gastric aspirate and external ear canal fluid from 67 newborns suspected of having sepsis acquired *in utero* or during birth were compared as aids to making an early diagnosis of this infection. All specimens were obtained within the first 18 hours of life. Of the 8 infants found to have a positive blood culture for sepsis, all had ear-canal cultures yielding the same pathogen as the blood specimen. Additionally, gastric aspirates in 7 of the 8 yielded organisms identical to those found in the blood. This good correlation, with 7 of the 8 septic infants showing polyps in both locations, suggests that microscopic examination of gram-stained smears from both sources can greatly assist the physician in making the early diagnosis of sepsis which is so essential to correct therapy. (10 refs.) - *N. Mize.*

Boston Hospital for Women
Boston, Mass. 02115

2017 **KANDALL, STEPHEN R.; DAVIS, THOMAS C.; & *ABRAMOWICZ, MARK.** Ampicillin failure in H. influenzae meningitis. *Clinical Pediatrics*, 11(5):264-267, 1972.

Apparent treatment failure with ampicillin in the case of a 6-mo-old girl with *H. influenzae* meningitis necessitated a switch, after 10 days of intravenous and intramuscular ampicillin treatment, to a penicillin and chloramphenicol combination. With this new regimen the child's temperature returned to normal and recovery was uneventful. While chloramphenicol is associated with some toxicity, the growing number of reported instances of late treatment failures with ampicillin suggests that the older combination regimen may, in fact, be preferable in cases where the *H. influenzae* organism is involved. After reviewing this report, however, 2 commentators have expressed skepticism, calling attention to the rudimentary nature of the recorded bacteriologic data and to the unusual feature of a positive culture after 24 hrs of therapy, a finding which should have provoked the search for some sequestered focus rather than an automatic switch to a different antibiotic. (11 refs.) - *N. Mize.*

*Albert Einstein College of Medicine
Bronx, N.Y. 10461

2018 **FAMILUSI, J. B.; MOORE, D. L.; FOMUFOD, A. K.; & CAUSEY, O. R.** Virus isolates from children with febrile convulsions in Nigeria. *Clinical Pediatrics*, 11(5):272-276, 1972.

Clinical and laboratory study of 105 Nigerian children with febrile convulsions and normal CSF findings has uncovered the frequent involvement of viruses, especially enteroviruses and arboviruses, in the pathogenesis of the fever-induced seizures. Twenty-three viral agents were isolated from 19 of the children, who ranged in age from 3½ mos to 5 yrs. The disease pattern in these children was typical of that generally associated with febrile convulsions in the area, with symptoms characteristic of upper respiratory tract infections being most common. Because of the small number of cases involved and problems with the selection criteria, however, any general conclusions regarding disease patterns caused by the isolated viruses will need to come from more extensive studies. (16 refs.) - *N. Mize.*

University College Hospital
Ibadan, Nigeria

2019 **FLANDERS, RAYMOND W.; PERSON, DONALD A.; ORREN, JERRY M.; ADAMS, JAMES M.; & RAWLS, WILLIAM E.** Is herpes simplex infection of the newborn preventable? *Clinical Pediatrics*, 11(5):293-294, 1972.

A cesarean section performed at term in a 19-year-old black woman with a genital herpes simplex infection (HSV 2) successfully prevented the infection of the newborn usually acquired in such cases during passage through an infected birth canal. Despite extensive efforts to isolate HSV, the infant has remained free of detectable infection and exhibited no antibody rise. In other cases where cervical herpetic lesions are evident, the cesarean mode of delivery should be considered as well. (3 refs.) - *N. Mize.*

Baylor College of Medicine
Houston, Texas 77025

2020 **LISCHNER, HAROLD W.; SHARMA, MANJIT K.; & GROVER, WARREN D.** Immunologic abnormalities in subacute sclerosing panencephalitis. *New England Journal of Medicine*, 286(14):787-788, 1972. (Letter)

The recent series of conflicting observations by different investigators regarding the immunologic responses of patients with subacute sclerosing panencephalitis may be attributable to several factors. Coherent explanations for the discrepant observations would include the possible inducement of immunosuppression by relative malnutrition, by infection with other viral agents, or by drugs in the SSPE patients studied by Gerson and the possibility of contaminating tissue antigens causing an apparent responsiveness to measles antigen in some of the other case reports. Additionally, the failure to achieve reproducible results in some of the *in vitro* assays reported may well stem from the impurity, variability, or instability of the antigens available. Subsequent studies in this area should further investigate these possibilities. (10 refs.) - *N. Mize.*

St Christopher's Hospital for Children
Philadelphia, Pa.

2021 **MONIF, GILLES R. G.** Rubella vaccination. *Obstetrics and Gynecology*, 39(2):304-307, 1972. (Editorial)

The long-range effects of current rubella vaccination programs, directed primarily toward the massive immunization of children, may well produce an adult population of childbearing age which is relatively immune, not to actual disease, but to significant viremia and hence to possible congenital infection. While this may contribute significantly to the ultimate eradication of congenital rubella, many in the critical target population—women of childbearing age—are not now being reached. While the risks involved in direct vaccination of this group are well known, the careful selection and monitoring of a vaccine population to assure against the accidental immunization of a pregnant woman can make this procedure a relatively safe one. This is especially true where vaccination can be done in the immediate postpartum period. (21 refs.) - *N. Mize.*

University of Florida College of Medicine
Gainesville, Fla. 32601

2022 **PRICE, D. J. E.; & SLEIGH, J. D.** Klebsiella meningitis-report of nine cases. *Journal of Neurology, Neurosurgery, and Psychiatry*, 35(6):903-908, 1972.

Antibiotic resistant *Klebsiella aerogenes* was recovered from 12% of the patients in the intensive care ward, and during the epidemic, 9 patients with head injuries or neurosurgery developed *Klebsiella* meningitis. The disease developed within 3 to 10 days of the time of suspected pathogen entry. *Klebsiella* was isolated from the throat or sputum before or at the same time as it was found in the cerebrospinal fluid. The disease had the clinical features of purulent meningitis in neurosurgery patients. Prophylactic ampicillin and cloxacillin had been given to 7 of 9 as a matter of common practice. Five of 9 received gentamicin and colistin therapeutically, and recovered. The others were diagnosed immediately prior to or after death. Withdrawal of prophylactic and therapeutic antibiotics resulted in the disappearance of *Klebsiella* from the unit and reduction in the infection rate. The prompt systemic, lumbar thecal, and intraventricular administration of colistin and gentamicin is the recommended therapy. (16 refs.) - *V. J. Goldberg.*

Killearn Hospital
Glasgow, Scotland

2023 **GIORGINI, GINO L., JR.; *HOLLINGER, F. BLAINE; LEDUC, LESLIE; ISSARESCU, S.; GEORGE, JACK; BLACKMAN, ALDEN; & THAYER, WALTER R., JR.** Radioimmunoassay detection of hepatitis type B antigen: A prospective study in blood donors and recipients. *Journal of the American Medical Association*, 222(12):1514-1518, 1972.

The incidence of hepatitis type B antigen (HBAg) in a donor population and the incidence of icteric and anicteric post-transfusion hepatitis among recipients of this transfused blood was investigated. During the study period 2,861 transfusions were administered to 318 recipients; HBAg was detected in 2 donor units by double diffusion in gel technique (AGD) and counterimmunoelectrophoresis (CIE), an incidence of 0.7 positive units per 1000 tested. Among the 101 CIE-negative donor bloods administered to 6 recipients who subsequently developed hepatitis, an additional 10 HBAg-positive units were detected by the more sensitive double antibody radioimmunoassay (RIA-DA) technique. Of 161 recipients who were followed up, 7 developed biochemical and/or histological evidence of viral hepatitis. The incidence of icteric hepatitis in these 161 patients was 2.4% whereas the total incidence of post-transfusion hepatitis was 4.3%. The results of this study establish a definite risk in transfusing blood which is considered negative by less sensitive methods; presently recommended techniques should be used for screening procedures in blood banks. (27 refs.) - *A. C. Schenker.*

*Baylor College of Medicine
Houston, Texas 77025

2024 **BRODSKY, ALAN L.** Atypical measles: Severe illness in recipients of killed measles virus vaccine upon exposure to natural infection. *Journal of the American Medical Association*, 222(11):1415-1416, 1972.

During an epidemic of measles in Aberdeen, SD, 5 cases of atypical measles occurred among recipients of killed measles virus vaccine. The clinical picture in these cases was characterized by vesic-

ular, intensely pruritic rashes beginning on the wrists and feet with a duration of 5-10 days. The 4 vaccinees who developed pneumonia were hospitalized due to severe illness with temperatures of 40-40.5°C. The immunological mechanism involved in this illness is thought to represent a cell-mediated, delayed-type hypersensitivity related to viral antigen or to tissue components derived from the host cell in which the measles vaccine virus is propagated. Because of the resurgence of measles in the USA, physicians are alerted to this possible complication. (9 refs.) - *A. C. Schenker.*

University of Texas
Southwestern Medical School
Dallas, Texas 75235

2025 **SHACKELFORD, PENELOPE G.; BOBINSKI, JOHN E.; *FEIGIN, RALPH D.; & CHERRY, JAMES D.** Therapy of *Haemophilus influenzae* meningitis reconsidered. *New England Journal of Medicine*, 287(13):634-638, 1972.

A retrospective study of 136 ampicillin (A)-treated and 116 chloramphenicol (C)-treated *Haemophilus influenzae* meningitis patients showed 2 groups to be well matched with regard to age, duration of symptoms before treatment, and initial CSF findings. A-treated patients remained febrile significantly longer and had significantly higher fevers than C-treated patients. CSF findings 7-12 days after the therapy was started were not significantly different. The death rates were comparable for both groups (6 of 136 and 8 of 116 for A and C-treated patients, respectively); 6 A-treated but no C-treated patients had relapses and 4 additional A-treated cases had slow bacteriological response. A significantly higher incidence of maculopapular rash occurred among A-treated patients. (26 refs.) - *V. J. Goldberg.*

*St. Louis Children's Hospital
St. Louis, Mo. 63110

2026 **MORRISON, JOHN C.; WHYBREW, D. W.; WISER, W. L.; BUCOVAZ, E. T.; & *FISH, STEWART A.** Laboratory characteristics in toxemia. *Obstetrics and Gynecology*, 39(6):866-872, 1972.

The RBC content and the concentrations of glucose, protein, uric acid and pH were measured in antenatally-obtained CSF and serum in an effort to discover correlations with the clinical findings of eclampsia. Of 9 women experiencing seizures during labor, all had increased CSF glucose and decreased Ca^{+2} as compared to 35 normal pregnant and non-pregnant controls. Ten with hypertensive vascular disease had normal serum and CSF parameters. Of 25 with preeclampsia, 14 had elevated serum uric acid levels and 5 of these had decreased serum pH. Of 21 with eclampsia, 19 had RBC in the CSF (in numbers correlated with clinical severity), and 14 had increased CSF glucose; all had increased CSF protein and uric acid and decreased CSF pH (which did not correlate with clinical severity). These findings suggest that the blood brain barrier is disrupted, allowing some proteins from the injured cerebral cells to escape. The changes in pH and glucose may be related to anoxia during convulsions. (15 refs.) - *V. J. Goldberg.*

University of Tennessee School of Medicine
Memphis, Tenn 38103

2027 **BLIGH, A. S.; WEAVER, C. M.; & WELLS, C. E. C.** Isotope encephalography in the management of acute herpesvirus encephalitis. *Journal of Neurology, Neurosurgery, and Psychiatry*, 35(5):569-581, 1972.

In 1 of 2 cases of necrotizing encephalitis, *Herpesvirus hominus* was isolated from the brain in biopsy material, and in the other case, infection was indicated by the diagnostic rise of serum antibody. Necrotizing encephalitis was suspected in both cases because the illness was grave, and focal signs developed in conjunction with radiological and EEG evidence of circumscribed lesions of the hemisphere. Serial scanning with technetium 99m pertechnetate was correlated with the clinical course of the illness, and anticipated by days focal epilepsy and other signs of relapsing infection. Increased isotope uptake may also indicate repair, so the changes must be viewed cautiously. Case 1 was treated with 0.3mg/kg/day cytarabine and idoxuridine but with poor results (patient is MR, hemiplegic, and epileptic). Case 2 received 3.5mg/kg/day cytarabine and dexamethasone simultaneously and recovered. A third patient had increased technetium uptake in the frontal and temporal lobes.

At autopsy, a diagnosis of necrotizing encephalitis was made, but herpes infection was not confirmed. (79 refs.) - *V. J. Goldberg.*

Cardiff Royal Infirmary
Cardiff, Wales

2028 **MCCALLIN, PAUL F.; FUCCILLO, DAVID A.; LEY, ANITA C.; GILKESON, MARY R.; TRAUB, RENEE; & *SEVER, JOHN L.** Gammaglobulin as prophylaxis against rubella-induced congenital anomalies. *Obstetrics and Gynecology*, 39(2):185-189, February 1972.

The results of a 1-year study involving a total of 1,045 Hawaiian women, initially examined for rubella during the first 8 weeks of pregnancy, show no clearcut evidence that the incidence of seroconversion was reduced by the prophylactic administration of either high or low titer gammaglobulin. Of 83 women exposed to rubella and given 20ml of gammaglobulin, none developed clinical rubella, 5 experienced seroconversions, and none delivered infants with congenital anomalies attributable to the infection. Of the 949 other patients not reporting rubella exposure during the first trimester, 34.2% were susceptible. The low frequency of actual infection among this susceptible group, only 6.7%, and the fact that only one of these women delivered a congenitally affected child prohibits drawing any meaningful conclusions as to gammaglobulin's actual prophylactic value. (8 refs.) - *N. Mize.*

*National Institutes of Health
Bethesda, Md. 20014

2029 **LUBY, JAMES P.; & SHASBY, D. MICHAEL.** A sex difference in the prevalence of antibodies to cytomegalovirus. *Journal of the American Medical Association*, 222(10):1290-1291, 1972.

A statistically significant sex difference in the prevalence of complement fixation (CF) antibodies to cytomegalovirus (CMV) is reported among a community of nonwhite persons in Dallas. Blood specimens were collected from 86 males and 109 females. CMV-CF antibody test titers $\geq$ 1:8 were found in sera from 88 Ss (45.1%). The prevalence of CF antibodies to CMV increased progressively with age for both men and women. In each age group, and particularly in the child-bearing age range (15-44 yrs), CMV antibody rates for women exceeded those for men. For the entire sample, CMV-CF antibodies in women were 55.0% as opposed to 32.6% for men ($P < .005$). The fact that men in this community were relatively isolated from child caring activities suggests that exposure to children might be an important determinant, though this has not been substantiated. The magnitude of the difference by sex in CMV antibody prevalence found in this study suggests that additional modes of virus transmission may exist. (10 refs.) - *A. C. Schenker.*

University of Texas
Southwestern Medical School
Dallas, Texas 75235

2030 **BASTIAN, F. O.; RABSON, A. S.; YEE, C. L.; & TRALKA, T. S.** Herpesvirus hominis: Isolation from human trigeminal ganglion. *Science*, 178(4058):306-307, 1972.

The possibility that herpesvirus hominis (HSV) produces latent infection in man was investigated by attempting to isolate this virus from the trigeminal ganglia obtained at autopsy from 23 humans. Explants of the ganglia were placed directly on monolayers of cells susceptible to lytic infection by HSV and the cultures were observed for cytopathic effects. Virus was recovered from 2 ganglia; no viruses were recovered from samples of choroid plexus. After tissues from one patient (with no clinical sign of herpes) were cultured for 3 weeks, areas of rounded refractile Vero cells were noted around the ganglionic explants. Electron microscopy of infected Vero cells showed typical herpesvirus particles. A second virus isolation was made from the trigeminal ganglion of a 54-year-old woman with malignant lymphoma. It is possible that the virus may be latent in only focal areas of the ganglia. (15 refs.) - *A. C. Schenker.*

National Cancer Institute
Bethesda, Maryland 20014

2031 **MARTINEZ, A. JULIO; HANISSIAN, A.; JABBOUR, J. T.; & DUENAS, D.** Rubella vaccine myositis. *Neurology*, 22(4):424-425, 1972. (Abstract)

Left leg pain and immunologic reaction, resulting from rubella vaccine immunization (MSD Meruvax duck cell type), is reported in a 6-year-old Negro boy. He was admitted 3 weeks after the immunization with a maculopapular rash about his face, shoulders and arms, fever, anorexia, lethargy, headaches, and alopecia. Laboratory studies revealed: a WBC of 28,000; mild anemia; markedly elevated SGOT (24-1760 units); LDH, 900-5000 units; aldolase, 16-21 units; CPK, 25 units. The LDH isoenzymes indicated severe muscle disease. The serum enzymes returned to normal with steroid therapy. Overall, the hospital course suggested an Arthus phenomenon, serum sickness or severe allergic or immunologic reaction. - *A. C. Schenker.*

2032 **ROSE, ARTHUR L.; & JOHNSON, ANNE B.** Bilirubin encephalopathy: Neuropathological and histochemical studies in the Gunn rat model. *Neurology*, 22(4):420-421, 1972. (Abstract)

Jaundiced homozygotes, survivors from jaundiced Gunn rats 14-18 days old, were studied for neurological deficits. The cerebellums were either normal in size or atrophic. Extensive neuronal degeneration and a general pattern of marked accumulation of intraneuronal glycogen was seen in the globus pallidus, posterolateral thalamus, Purkinje cells, and brainstem nuclei. Cerebellar cortex showed extensive degeneration of Purkinje cells with cytoplasmic vacuoles and basophilic cytoplasmic granules. In one very atrophic cerebellum, some of the Purkinje cells and their dendrites were replaced by amorphous material that stained with Sudan black B and was not extractable with acetone. Acid phosphatase reactions were strongly positive around the periphery of these lesions. It is suggested that if the neurotoxicity of bilirubin is due to an uncoupling of oxidative phosphorylation, the negative reduced pyndine nucleotide (DPNH) and succinate dehydrogenase findings indicate that its effect is not exerted in the initial phases of electron transport. - *A. C. Schenker.*

2033 **FRANGENBERG, E. E.; HORNER, F. A.; & FILOMENO, A. R.** Roseola infantum and its modes of central nervous system involvement. *Neurology*, 22(4):419-420, 1972. (Abstract)

A possible causal relationship between roseola infantum and permanent central nervous system (CNS) disorders was investigated by re-examining 82 hospital records of documented pediatric roseola cases. After exclusion of other antecedent noxious influences, 25 instances in which CNS signs could be related to roseola were found. A bulging fontanelle, convulsions, and hemiparesis were found most frequently as transient features. Recurrent epileptic seizures, persistent hemiparesis, or global psychomotor retardation occurred singly or in combination in 8 children. Neurological signs were seen in most cases during the clinical course of roseola. If they do not occur in the acute phase of the illness or within 2 weeks thereafter, a deficit is unlikely. - *A. C. Schenker.*

2034 **PETERS, ALLEN H.; O'GRADY, JEANNE E.; & MILANOVICH, ROBERT A.** Aseptic meningitis associated with echovirus type 3 in very young children. *American Journal of Diseases of Children*, 123(5):452-456, 1972.

Of eighty cases of aseptic meningitis occurring in Richmond, Va., among poor black children between June and October 1970, 21 were age 6 mos or less, two-thirds were age 5 yrs or less, and the oldest was 12 yrs old. The most frequent clinical findings were fever, stiff neck, vomiting, and irritability and lethargy among infants. Echovirus type 3 was isolated from the CSF of 17 patients. The clinical attack rate for household contacts was only 3% but serum neutralization results strongly suggest that siblings and parents may have transmitted the virus. Echovirus type-3 had not been previously isolated in Virginia and was not found again in selected spinal fluid samples 2 mos after the epidemic had run its course. (23 refs.) - *V. J. Goldberg.*

Southern California Permanente Medical Group
Bellflower, Calif. 90706

2035 **YOUNG, LOWELL S.; LAFORCE, F. MARC; HEAD, J. JAMES; FEELEY, JAMES C.; & *BENNETT, JOHN V.** A simultaneous outbreak of meningococcal and influenza infections. *New England Journal of Medicine*, 287(1):5-9, 1972.

An outbreak of 11 cases (3 fatal) of Group B, sulfonamide-resistant *Neisseria meningitidis* infec-

tions occurred during a 9-day period among 55 elderly inst women in a single ward. Meningococci were isolated from 4 carriers in the affected ward. All carriers and survivors of systemic infection had 4-fold rises in titers to Group B antigens. Twenty-four of 50 from the affected ward and 19 of 49 from an unaffected ward had 4-fold rises in influenza antibody. Five of 8 with meningococcal infection and 4 carriers had evidence of influenza infection (a significant correlation in the latter case). Influenza virus may enhance the likelihood that a host will acquire meningococci after exposure to these bacteria. (13 refs.) - *V. J. Goldberg.*

*Center for Disease Control
Atlanta, Ga. 30333

2036 **NI, LOUISA Y.; SHOFF, JANET; & LAMA, SHARI.** Hepatitis-B antibody in volunteer blood-donors. *Lancet*, 2(7785):1035, 1972. (Letter)

Screening of a large number of volunteer blood donors for hepatitis-B antibody (anti-HBAg or HBAb) revealed detectable HBAb activity in 106 (4.2%) of 2492 by passive hemagglutination assay, the titers ranging from 1/5 to > 1/6400, in only 3 (0.012%) by counterelectrophoresis, and in none by agar-gel diffusion. Twenty (0.8%) were demonstrable by use of 'Rheophoresis' kits, all with passive hemagglutination assay titers > 1/160. The frequency of antibody to HBAg previously reported among voluntary blood donors as measured by the radioimmunoprecipitation test was 14.4%. (3 refs.) - *B. J. Grylack.*

American National Red Cross National
Headquarters
Washington, D. C. 20006

2037 **ANDERSON, J. M.; & NICHOLLS, M. W. N.** Herpes encephalitis in pregnancy. *British Medical Journal*, 1(5800):632, 1972.

A 19-yr-old woman died of herpes encephalitis 5 days after delivering a live full-term infant. Since the infant had no serum antibodies to herpes simplex or clinical symptoms at age 23 days and the mother had no serum antibodies, it is unlikely that the virus was spread by the bloodstream. The necropsy findings of olfactory bulb, olfactory tract, and hippocampa necrosis, and isolation of virus from the temporal lobe support the hypothesis that the virus was spread by the direct neural route. (2 refs.) - *V. J. Goldberg.*

Midland Centre for Neurosurgery and Neurology
Smethwick, Worcs, England

2038 Herpes encephalitis. *British Medical Journal*, 1(5800):582-583, 1972. (Editorial)

Herpes acute necrotizing encephalitis may be the most common form of sporadic fatal encephalitis affecting neonates and young adults. The virus may gain access to the brain via neural or hematogenous routes. Diagnosis is difficult because the disease is characterized initially by influenzalike symptoms, and the neurological findings are unspecific. EEG may be helpful, but there is no EEG pattern characteristic of this disease. Diagnosis depends on the identification of herpesvirus in brain tissue (determined by immunofluoresence or by culture), as antibody assay is inconclusive and the virus is not usually found in the CSF. New approaches include changes in the electrophoretic properties of CSF proteins. Prompt diagnosis is necessary because treatment by idoxuridine or by cytarabine must be given early to have effect. (45 refs.) - *V. J. Goldberg.*

2039 **SCANLON, JOHN.** Human fetal hazards from environmental pollution with certain non-essential trace elements. *Clinical Pediatrics*, 11(3):135-141, 1972.

Reliable scientific evidence regarding the influence of trace metals and other environmental pollutants on the developing fetus is extremely limited. Most scientific interest to date has concentrated on lead and mercury, though cadmium, titanium, nickel, tin and arsenic merit investigation, as well as possible human teratogens. Further research in this extremely important area will need to consider carefully the genetic background of the fetus and will, additionally, need to develop other measures of fetal damage to supplement the traditional ones of stillbirth rate, neonatal mortality, and specific patterns of congenital malformation. The significant potential hazards to the fetus represented by greatly increased levels of environmental pollution make

this investigation an urgent priority. (41 refs.) - *N. Mize.*

Boston Hospital for Women
Boston, Mass. 02115

2040 **KUSHNICK, THEODORE.** An infant with acute fever and nondescript rash. *Clinical Pediatrics*, 11(5):309, May 1972.

A 5-mo-old boy was hospitalized with severe episodic abdominal pain, marked irritability, a temperature of 103.2, and a fresh erythematous rash over the trunk and proximal extremities. Despite normal CSF findings on lumbar puncture and the nondescript rash, laboratory analysis of a blood culture showed it to be positive, containing Gram negative diplococci. On this basis a diagnosis of meningococcemia and meningococcal meningitis was made. Complete recovery followed antibiotic treatment. - *N. Mize.*

New Jersey College of Medicine and Dentistry
Newark, N.J.

2041 **ZIAI, MOHSEN; & *KUSHNICK, THEODORE.** Recurrent meningitis. *Clinical Pediatrics*, 11(5):308-309, 1972.

An unusual case of recurrent *E. coli* meningitis in a 3-yr-old boy spurred the search for some communicating channel between the external body surface and the central nervous system. Initially, a dermal sinus tract, discovered by an intrathecal dye study, was thought to be responsible and was surgically excised. When the *E. coli* meningitis returned 1 month later, another explanation was sought. This time, the surgical removal of a congenital dermoid tumor, situated intraspinally and chronically infected, ended the boy's meningitis attacks. (2 refs.) - *N. Mize.*

*New Jersey College of Medicine
Newark, N.J.

2042 **POPPER, HANS; & *MACKAY, IAN R.** Relation between Australia antigen and autoimmune hepatitis. *Lancet*, 4(7761):1161-1163, 1972.

Consistent with recent observations on the hepatitis-B-associated antigen (Australia antigen) and autoimmunity in chronic hepatitis, it is assumed that autoimmune hepatitis is a disease peculiar to infection with hepatitis-B virus. Immunologically, if this is correct, the disease would be mediated either by a persistent infection with replication of the virion in hepatocytes or by an aggressive autoimmune reaction against specific host protein components originally incorporated into the B-antigen particle. (27 refs.) - *N. Mize.*

*Royal Melbourne Hospital
Victoria 3050, Australia

2043 **BJORNEBOE, M.; & PRYTZ, H.** Relation between Australia antigen and autoimmune hepatitis. *Lancet*, 1(7764):1335-1336, 1972. (Letter)

The general hyperstimulation of the immune system—recently singled out by Professors Popper and Mackay as the possible cause of the persistent autoimmune reaction with accompanying hypergammaglobulinemia characteristically associated with B-antigen-positive hepatitis—may well be due to the failure of the diseased liver in its normal role as an inhibitor of immunogens. If this hypothesis is correct, the high immunoglobulin concentration in chronic liver disease would be caused not by an excess of antigens, but instead by the loss of inhibition of the immunogenic effect of these antigens as they are absorbed from the gut. Such a relationship would be consistent with other experimental observations in this area. (12 refs.) - *N. Mize.*

Bispebjerg Hospital
Copenhagen NV, Denmark

2044 **HADZIYANNIS, ST.; VISSOULIS, CH.; MOUSSOUROS, A.; & AFROUDAKIS, A.** Cytoplasmic localisation of Australia antigen in the liver. *Lancet*, 1(7758):976-979, 1972.

The results of a systematic immunofluorescence study of Au antigen in the liver of 22 apparently healthy Au-antigen carriers and of 9 seropositive patients with liver disease support the view that Au antigen may be a virus-coat material produced in excess in the cytoplasm of liver cells. If this is correct, its presence in the liver would be unrelated to any cytopathic effects of hepatitis virus B. While the localization of Au antigen in

the cytoplasm of hepatocytes was observed both in carriers and in the seropositive patients with liver disease, the normal liver of carriers appeared to contain significantly more Au antigen as judged by the intensity and number of fluorescent cells. These findings are compatible with the suggestion that Au antigen carriers may have a balanced or slow-virus infection which produces large amounts of Au antigen but few or no actually infectious viruses. (20 refs.) - *N. Mize.*

Hippokration General Hospital
Athens, 610, Greece

2045 Seeking the answers to phototherapy with newborn infants. *Clinical Pediatrics*, 11(10):557, 1972.

While phototherapy is a widely accepted treatment for incipient jaundice or hyperbilirubinemia in the newborn, many uncertainties about the procedure remain. A new 2-year cooperative study under the guidance of the National Research Council will attempt to resolve some of these outstanding questions and will launch specific investigations into such areas as optimal technics, safety, and the biologic mechanisms at work in the infant during phototherapy. - *N. Mize.*

2046 Subacute sclerosing panencephalitis (SSPE). *Clinical Pediatrics*, 11(11):610, 1972.

The first report of the nationwide SSPE Registry, initially established in 1969, has just been released. Survey findings show the approximate incidence of SSPE, a chronic progressive disease of the central nervous system, to be one per million in the childhood population from 1960-70. Patients, a high percentage of whom were clustered in the southeastern United States, ranged in age from 2 to 21 yrs, with 7.2 yrs as the mean. Males were predominant. (3 refs.) - *N. Mize.*

2047 ZOUMBOULAKIS, DIMITRI; KARABOULA, KATHERINE; ALBANIS, VLASSIS; & KIOSSOGLOU, KOSMAS, A. Meningitis due to Escherichia Coli 0126:B16. *Clinical Pediatrics*, 11(10):603-604, 1972.

A rare case of meningitis due to *E. coli* has been identified as the cause of death in a 14-yr-old girl. The disease ran an extremely stormy course and despite antibiotic treatment, the girl died 40 days after disease onset. Since *E. coli* of the same type as that found in the CSF was recovered from the child's stools, it is suspected that the meningitis was related to a chronic constipation associated with a huge fecal mass in the umbilical region. (9 refs.) - *N. Mize.*

St Sophie's Children's Hospital
Goudi (608), Athens, Greece

2048 MARTIN, GILBERT I.; & DEGRINNEY, JOSEPH T. Intrafamilial infection with *Neisseria meningitidis*, Group C. *Clinical Pediatrics*, 11(9):538-540, 1972.

A rare outbreak of meningococcal infection within one family living on a military installation has been attributed to a sulfonamide-resistant Group C meningococcus, *Neisseria meningitidis*. Of the 7 family members examined after the initial case was diagnosed, two were found to have meningococcal meningitis, one had clinical meningococcemia, and two were nasopharyngeal carriers. Serum immunoglobulins were within normal limits. The patients all responded to intravenous penicillin and recovery was uneventful. Of particular epidemiologic interest is the fact that all 3 children who developed clinical disease shared the same bedroom. Reports of such simultaneous infection within one family are extremely rare in the literature. (12 refs.) - *N. Mize.*

USAF Hospital
Loring Air Force Base
Maine 04750

2049 MCDONALD, ROBERT. Purulent meningitis in newborn babies: Observations and comments based on a series of 82 patients. *Clinical Pediatrics*, 11(8):450-454, 1972.

Eighty-two cases of purulent meningitis in newborn babies under 4 wks of age were diagnosed on the basis of cultured organisms from an abnormal cerebrospinal fluid or low CSF sugar

level and were closely observed over the course of the infection. Generally, the earlier the onset, the higher the death rate, with mortality overall averaging 50%. The high percentage of nonwhite babies in the series suggests that, in South Africa at least, these infants are more prone to develop the infection than are white babies. Early diagnosis and treatment, essential to preventing the neurologic and mental abnormalities characteristic of meningitis survivors, are hampered by the nonspecific nature of clinical features in this age group. As expected, adverse prognostic signs included hypothermia, convulsions, loss of consciousness, and onset of disease in the first week of life. Since rapid treatment is essential, an antibiotic combination of high dosage gentamycin, trimethoprimsulphamethoxazole, and penicillin is recommended as a generally appropriate therapy until precise bacteriological studies can be completed. (19 refs.) - *N. Mize.*

2050 CENTIFANTO, YSOLINA M.; DRYLIE, DAVID M.; DEARDOURFF, STEPHEN L.; & KAUFMAN, HERBERT E. Herpesvirus type 2 in the male genitourinary tract. *Science*, 178(4058):318-319, 1972.

Because antibodies to herpesvirus 2 are associated with early sexual activity and promiscuity and because epidemiologic studies indicate that genital herpes is venereally transmitted, a study was conducted to determine whether the male genitourinary tract could be a reservoir of herpesvirus. Ss comprised 190 males, ages 15 to 85 yrs, randomly selected from various socioeconomic classes and of a mixed racial composition. Of specimens collected from urethral swabs, prostate fluid, sections of vas deferens, prostate biopsies and foreskin tissue, 15% were positive for herpesvirus. There was no significant difference between age groups in the number of positive cultures. Overall, the data suggest that persistence of herpesvirus in the male genitourinary tract, even in the absence of overt disease, provides a reservoir for venereal transmission of the virus. (11 refs.) - *A. C. Schenker.*

College of Medicine
University of Florida
Gainesville, Florida 32601

2051 BEATTIE, A. D.; MOORE, M. R.; DEVENAY, W. T.; MILLER, A. R.; & GOLDBERG, A. Environmental lead pollution in an urban soft-water area. *British Medical Journal*, 2(5812):491-493, 1972.

Of 23 houses (mean age 26 yrs) receiving soft water through lead pipes, lead levels were below 100mg/liter in 7, and these houses were supplied by less than 60ft of lead pipe. Four of the 71 inhabitants of the 23 houses had blood levels greater than 40mg/100ml, and 3 of these lived in houses with lead-lined water storage tanks. Twenty-three had less than 415nmol PBG/10^{10} RBC/hr, and decreased aminolevulinic acid dehydrase correlated with household water lead content. (13 refs.) - *V. J. Goldberg.*

M. R. C. Group in Iron and Porphyrin Metabolism
StobHill Hospital
Glasgow, N.1 Scotland

2052 MURRAY, J. D.; FLEMING, P. C.; ANGLIN, C. S.; STEELE, J. C.; & FUJIWARA, M. W. Acute bacterial meningitis in childhood. *Clinical Pediatrics*, 11(8):455-464, 1972.

When properly managed as a medical emergency, the prospects for recovery from acute bacterial meningitis in childhood are excellent. Recent experience in Toronto, Canada, with a program for specific and supportive therapy in a series of 236 cases of purulent meningitis has seen the fatality rate reduced by three-quarters, to 2.9%. While certain specifics of the recommended antibiotic therapy will vary depending on allergies and on whether the disease occurs in childhood or in the neonatal period, ampicillin is generally the first treatment of choice. The relatively common practice of administering supplementary sulphonamides or other antibiotics is probably unnecessary and may in fact be harmful. Overall the major reduction in mortality and the prevention of complications can be primarily attributed to an intensive supportive therapy program which includes specific attention to adequate nursing care, control of fever, anticonvulsant drug therapy, and recent advances in the management of cerebral swelling and septic shock. (24 refs.) - *N. Mize.*

Hospital for Sick Children
Toronto 101, Ontario, Canada

2053 DAYAN, A. D.; GOODDY, WILLIAM; HARRISON, M. J. G.; & RUDGE,

PETER. Brain stem encephalitis caused by *Herpesvirus hominis. British Medical Journal*, 3(5837):405-406, 1972.

Two patients had brain stem encephalitis caused by *Herpesvirus hominus.* The first patient had appropriate antibody response, changes in the EEG, and typical pathology at necropsy. The other patient had serum antibody response and herpesvirus antigens in cells found in the CSF, and virus was isolated from the CSF. EEG and immunofluorescent detection of viral antigens in cells from the CSF are needed for rapid diagnosis and treatment with idoxuridine. (7 refs.) - *V. J. Goldberg*.

Institute of Neurology and National Hospitals for Nervous Diseases
London WC 1, England

2054 **MARGOLIN, FRED G.; & KANTOR, NEIL M.** Hemorrhagic disease of the newborn. *Clinical Pediatrics*, 11(1):59-60, 1972.

A recent case of neonatal hemorrhage successfully treated with vitamin K has been nearly conclusively related to maternal ingestion of an anti-epileptic drug, primadone, during pregnancy. Previously such cases have been reported in Europe, but only once in the American literature, probably because the administration of vitamin K is a routine procedure in most American newborn nurseries. While the precise relationship between anticonvulsant use in pregnancy and neonatal hemorrhage is not well understood, this most recent experience underlines the need for careful attention to the always high-risk pregnancies of epileptic women. Additionally, prophylactic vitamin K therapy should be routinely administered in the newborn period to all infants of epileptic mothers. (10 refs.) - *N. Mize.*

1390 Chambers Road
Denver, Colo. 80010

2055 **KAGWA-NYANZI, JUANITA A.; & ALPIDOUSKY, V. K.** Subaponeurotic hemorrhage in newborn infants. *Clinical Pediatrics*, 11(4):224-227, 1972.

Nine instances of subaponeurotic hemorrhage in newborn infants observed over a month's period at one Ugandan hospital call attention to the frequent occurrence of this condition among African newborns. Thrombotest measurements performed on 6 of the babies revealed deficiencies in several coagulation factors. Additionally, two of the infants developed hyperbilirubinemia. In line with previous reports, it seems clear that obstetric use of the vacuum extractor plays an important etiologic role in this condition. In the present series, 6 of the 9 infants were delivered by vacuum extraction and all 6 had low Thrombotest readings. (8 refs.) - *N. Mize.*

Makerere Medical School
Kampala, Uganda

2056 **JARVIS, CHARLES W.; & SAXENA, KRISHNA M.** Does prior antibiotic treatment hamper the diagnosis of acute bacterial meningitis? *Clinical Pediatrics*, 11(4):201-204, 1972.

Spinal fluid cultures and other laboratory findings in diagnosed meningitis patients were compared to determine the effect of prior antibiotic treatment on the diagnosis of acute bacterial meningitis. Of 135 children between 1 month and 15 yrs admitted to a Minnesota hospital over a 5-year period, 60 had received some type of antibacterial drug—usually penicillin—before the diagnosis was made. Little real difference between the "treated" and "untreated" groups was found. Laboratory results were comparable for both groups with respect to CSF cell counts, the identification of specific bacterial agents, blood cultures, and CSF glucose and protein values. Additionally, prior therapy was found to have no adverse effect on the response to treatment, duration of hospitalization, or ultimate outcome. Provided the clinician has a high index of suspicion and performs a lumbar puncture, the findings in this study indicate that prior antibiotic treatment does not hamper the diagnosis of meningitis. (7 refs.) - *N. Mize.*

The Children's Hospital
St. Paul, Minn. 55102

2057 Value of anti-Rh immunoglobulin in suppression of Rh immunization during pregnancies. *Clinical Pediatrics*, 11(4):194, 200, 1972.

The results of worldwide clinical trials involving

several thousand women have firmly established the positive value of anti-Rh immunoglobulin in the suppression of Rh immunization during pregnancy. All Rh-negative women who are not already immunized and who give birth to an Rh-positive infant should receive a dose of anti-Rh within 72 hours of delivery. If these recommendations were routinely followed throughout the world, the number of exchange transfusions required would fall drastically, and thousands of needless deaths would be prevented. (8 refs.) - *N. Mize.*

Medical School, Observatory
Cape Town, S. Africa

2058 ALAGILLE, DANIEL. Clinical aspects of neonatal hepatitis. *American Journal of Diseases of Children*, 123(4):287-291, 1972.

During the course of a 9-year study, 316 newborn infants with prolonged nonhemolytic jaundice were examined, of whom 54% had viral hepatitis, 29% showed anatomical malformations of the extrahepatic biliary ducts, and 17% had jaundice associated with a variety of causes. Analysis of the findings suggests that hepatitis occurs primarily in boys, whereas extrahepatic biliary atresia affects both sexes equally; stools become acholic sooner in cases of extrahepatic biliary atresia than in hepatitis; the general health of neonatal hepatitis infants is interfered with in only 20.9% of cases; and neurologic symptoms occur frequently (28.7%) in neonatal hepatitis, but only rarely in cases of extrahepatic biliary atresia. Since the presence of biliary thrombi in the portal space and identification of portal biliary angiomatosis h[illegible] proved of only limited value in distinguishing between the 2 conditions, however, and since both share many similar histological findings, immediate surgery for any case of prolonged cholestatic jaundice in infants may be the best way of preventing possibly irreversible ductal disease. (9 refs.) - *N. Mize.*

Hopital Parrot
Bicetre, France

2059 WEWALKA, FRIEDRICH G. Protracted and recurrent forms of viral hepatitis. *American Journal of Diseases of Children*, 123(4):283-286, 1972.

The course of 400 cases of icteric viral hepatitis was reviewed in order to identify possible correlations between Australian antigen (AuSH)-positive findings and the duration of bilirubin elevation, serum glutamic pyruvic transaminase levels, and various histologic findings. The jaundice in AuSH-positive patients was regularly unresponsive to corticoid treatment and tended to be of longer duration than that associated with other types. In 62 cases of chronic hepatitis, 53% were positive for AuSH. The ratio of corticoid treated to untreated cases in AuSH positive and negative cases was 11:7 and 2:9, respectively. Failure of the immune response may also be associated with chronicity. Cessation of glucocorticoid (prednisolone) treatment was frequently followed by the recurrence of symptoms and by the persistence of the AuSH antigen. (40 refs.) - *V. J. Goldberg.*

University of Vienna
Vienna, Austria

2060 MCCRACKEN, GEORGE H. The rate of bacteriologic response to antimicrobial therapy in neonatal meningitis. *American Journal of Diseases of Children*, 123(6):547-553, 1972.

CSF cultures in 38 infants, all less than 28 days old, showed the existence of bacterial meningitis to be caused by gram-positive organisms in 16 and by gram-negative organisms in 22. Of those with gram-positive organisms, 3 died, and 10 showed improvement within 48 hours of initiation of antibiotic therapy; the cerebrospinal fluid became sterile within 72 hrs in 12 of 13 cases. In contrast, of those with gram-negative infections, 4 died and 13 still had positive CSF cultures from 2 to 11 days after the initiation of therapy. Five of 6 with sterile first follow-up CSF cultures improved, and 12 of 13 with persistently positive CSF cultures remained symptomatic. The reason for this difference in bacteriologic response between gram positive and gram negative infants is unknown. Two yrs later, 2 of the 9 who have been followed up are completely normal and the others have sequelae ranging from delayed speech to severe MR. The recommended initial antimicrobial therapy is 100 or 200mg/kg/day of ampicillin for infants under and over 1 wk, respectively, plus 5 or 7.5mg/kg/day of gentamicin sulfate. The CSF should be cultured until it is sterile. The low mortality rate in this study

probably reflects prompt diagnosis and treatment, the small number of prematures, and aggressive attention to supportive care. (16 refs.) - *V. J. Goldberg.*

5323 Harry Hines Blvd.
Dallas, Texas 75235

2061 **KLOCK, LAWRENCE E.; SPOTSWOOD, L. SPRUANCE; BAILEY, ALTHEA; MCQUARRIE, HOWARD G.; HERBERTSON, RICHARD M.; SHARP, HOWARD C.; & SMITH, CHARLES B.** A clinical and serological study of women exposed to rubella vaccinees. *American Journal of Diseases of Children*, 123(5):465-468, 1972.

Paired blood samples were collected from 535 women prior to and 7 to 21 wks after a 2-day-long rubella immunization campaign during which 188,000 Utah children received the HPV-77 DK-12 vaccine. At the time of the immunization campaign, 326 of the women were pregnant and 85 were seronegative. In a group of 218 women with 1 to 11-yr-old vaccinated children, 33 were seronegative; 18 of these were pregnant. One of the pregnant, seronegative women had clinical rubella, seroconverted, and later bore a stillborn fetus, though it is probable that a wild-virus infection, not vaccine-virus induced rubella, was at fault. Findings among other groups of pregnant women, those with unvaccinated children and those with no children at home, were not significant. One seropositive woman experienced a rise in titer, and 52 seronegative women who had children at home failed to seroconvert. Since, with one possible exception, there was no transmission of virus from vaccinated children to their nonimmune mother, these findings support the concept that infection of a susceptible adult with rubella vaccine virus secondary to spread from a vaccinee is an unlikely event. (16 refs.) - *V. J. Goldberg.*

Center for Disease Control
Atlanta, Georgia 30333

2062 **MACCALLUM, FREDERICK O.** Hepatitis. *American Journal of Diseases of Children*, 123(4):332-335, 1972.

Serum hepatitis virus B is known to be spread parenterally, but the fecal/oral and oropharyngeal secretion droplet routes of infection need to be evaluated. Three sera assumed to contain virus B and the naso-pharyngeal washings from a hepatitis patient previously inoculated with a fourth virus B-containing serum were used to inoculate volunteers either subcutaneously or intranasally. With serum 1, 2 of 5 subcutaneously inoculated volunteers developed jaundice and symptoms within 54 to 70 days, while 2 of 5 of the intranasally inoculated volunteers developed the disease. After subcutaneous inoculation with serum 2, 6 of 11 developed biochemical evidence of the disease, but examination of the serum 25 yrs later revealed no virus particles or Australian antigen. With serum 3, 9 of 18 injected and none of 10 intranasally inoculated volunteers developed the disease. Virus particles were seen in the later electron microscopy of serum 3, but no Australian antigen was found. (8 refs.) - *V. J. Goldberg.*

Radcliffe University
Oxford, England

2063 **VASSELLA, FRANCO; & *ROSSI, ETTORE.** Neonatal hepatitis and cytomegalovirus. *American Journal of Diseases of Children*, 123(4):300, 1972.

Twenty-three of 43 cases of neonatal cytomegalovirus infection were determined by detection of virus and increases in serum antibody to be congenital. Of the 23 cases, 17 had hepatomegaly, 10 had splenomegaly, and 6 were jaundiced. There was good correlation between serum glutamic pyruvic transaminase (SGPT) and hepatomegaly. Cytomegalovirus infection was associated with increases in direct serum bilirubin and SGPT. Histologic findings of needle biopsies in 6 cytomegalovirus cases included cellular changes in 6, periportal and intracinic infiltration in 4, and intact lobular structure in 3. Cellular necrosis was found in 2 and giant cells in 1. Cytomegalic inclusion disease should be considered in the differential diagnosis of neonatal hepatitis. - *V. J. Goldberg.*

*University of Berne
Berne, Switzerland

2064 **PORTER, C. ANDREW; HAYNES, DAVID; MOWAT, ALEXANDER; & WILLIAMS, ROGER.** Etiologic factors in

neonatal hepatitis. *American Journal of Diseases of Children*, 123(4):300-301, 1972.

Of 15 cases of neonatal hepatitis, 8 have completely recovered; 7 have evidence of active disease, including 1 with cirrhosis. Six of 11 cases tested had Milan antigen, 3 of 9 were α_1-antitrypsin deficient, and 1 had cytomegalovirus. (2 refs.) - *V. J. Goldberg.*

King's College Hospital
London, England

2065 CHOIE, DAVID D.; & RICHTER, G. W. Lead poisoning: Rapid formation of intranuclear inclusions. *Science*, 177(4055):1194-1195, 1972.

Young adult female Sprague-Dawley rats weighing 220 to 270g were injected intraperitoneally with a single dose of lead (0.05 to 0.20mg per gram of body weight) and demonstrated intranuclear inclusions in 10% to 25% of epithelial cells in proximal tubules in the kidney within 1 to 6 days. This finding indicated that the development of the pathognomonic intranuclear inclusions in renal tubular epithelium represents an acute manifestation of lead poisoning. Increasing the dose of lead did not significantly change the percentage of proximal cells with intranuclear inclusions during the 6-day period. The origin of the intranuclear inclusions associated with lead poisoning is still uncertain. The protein component may be derived from a preexisting nucleoprotein or may be synthesized *de novo*. Cytoplastic structures composed of fibrillar and amorphous material and located only in proximal tubular epithelial cells of leaded rats may share a common precursor with the intranuclear inclusions, perhaps a soluble complex of protein and lead. (8 refs.) - *B. J. Grylack.*

University of Rochester Medical Center
Rochester, New York 14642

2066 GOLDSCHMIDT, M. N.; & BAILEY, D. W. Management of Reye's syndrome. *New England Journal of Medicine*, 287(5):255, 1972. (Letter)

The use of hyperventilation in patients with intracranial hemorrhage (Zervas, *N Engl J Med* 286:1075-1077, 1972) may be extended to the management of encephalopathies such as Reye's syndrome. The effects of hyperventilation may be the decrease of intracranial blood volume (and consequently the decrease of intracranial pressure), and the resulting alkaline state may enhance cerebral metabolism in the presence of hepatic toxins. The hyperventilation and hyperemesis of Reye's syndrome may be protective responses to the encephalopathy. Hyperventilation should be supported, and the possible role of alkali infusion should be investigated. (2 refs.) - *V. J. Goldberg.*

National Naval Medical Center
Bethesda, Maryland

2067 COLON, A. R.; & SANDBERG, D. H. Hepatic encephalopathy treated with L-Dopa, recovery followed for 18 months. *Pediatrics*, 51(6):1105, 1973. (Letter)

A 13-year-old girl with hepatic encephalopathy (HE) has been successfully treated with L-Dopa. The Negro girl was admitted with a one-year history of urinary tract infections, anasarca, and ascites. Hematuria was observed, a low serum protein and reversed A:G ratio, and low hemoglobin (5.6gm/100 ml). Liver biopsy revealed chronic active hepatitis and renal biopsy showed membrane glomerulonephritis. Prednisone therapy was not effective for any length of time. She gradually lapsed into hepatic coma, and at this time she was given 750mg L-Dopa by nasogastric tube every 8 hours. After 18 hr, the patient was fully alert and oriented, and improved rapidly with reduced medication and continued to do well after 72 hr, when the medication was stopped. A follow-up for 18 months revealed no recurrence of HE. Treatment of hepatic coma with L-Dopa is based on the hypothesis that false neurochemical transmitters accumulate in HE and inhibit competitively normal neurotransmission. (3 refs.) - *A. C. Schenker.*

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Miami, Florida 33152

2068 DELORIMIER, ALFRED A. Surgical management of neonatal jaundice. *New England Journal of Medicine*, 288(24):1284-1286, 1973.

The diagnosis of obstructive jaundice in infants is discussed, and an abbreviated diagnostic process is outlined. Virus infection in the mother, such as rubella, hepatitis, or genital herpes, must be ruled out. Infants with hepatitis tend to have an enlarged liver with a sharp edge that is not as hard as the liver with biliary atresia. Microcephaly, hydrocephaly, seizures, and choreoretinitis suggest toxoplasmosis or cytomegalic inclusion disease. Laboratory tests include X-ray studies, liver function tests (a consistently falling direct bilirubin suggests cholestasis); and percutaneous prolonged partial asphyxia by mechanical regulation of the constriction of the maternal abdominal aorta. Lowering of the arterial blood pressure in the distal portion of the maternal aorta by constriction of this vessel higher up resulted in impairment of placental intervillous space perfusion by maternal blood. Diminished intervillous space perfusion, in turn, led to a partial asphyxia of the fetus *in utero*. The fetuses were anesthetized controls, animals with asphyxia to a derived mean pH between 7.00 and 7.07, and animals with asphyxia to a derived mean pH below 7.00. At the end of a standard 3-hour insult period, the fetus was delivered and samples of cerebral cortex, caudate nucleus, corpus callosum, cerebellar cortex, and cerebellar peduncles were removed. Grossly apparent brain swelling was absent, shifts in water content were not pronounced, and tissue necrosis was evident in only 2 instances when it was highly restricted in its distribution. The finding that samples of cortex away from the necrotic patches in the 2 animals in which necrosis was present exhibited water content for the asphyxiated group as a whole underlined the fact that the degree of swelling produced here was separate from and premonitory to the degree of swelling associated with tissue necrosis. When significant differences in electrolyte content occurred, the reduction in sodium and potassium contents of brain tissues were of the order of 10 to 30%, with reductions in sodium tending to be more marked than those in potassium. It was predominantly the gray matter that exhibited shifts in water and electrolytes, the cerebellar cortex being the most affected. (13 refs.) - *B. J. Grylack.*

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MEDICAL ASPECTS—Trauma or Physical Agents

2069 **SAMPSON, PAUL.** Medical progress has little effect on an ancient childhood syndrome. *Journal of the American Medical Association*, 222(13):1605-1612, 1972. (Editorial)

The physician's role in treating the estimated 60,000 annual cases of the battered child syndrome was reviewed by a panel of specialists with professional experience in this area. The panelists emphasized that nobody can predict situations where this may occur; that prevention amounts to removing the child from an abusive home; that physicians are either unwilling or unable to recognize the signs of such abuse; and that without preventive measures such children are in danger of brain damage or death. However, on the positive side it is possible to identify child abuse by means of roentgenograms; physicians enjoy virtually absolute immunity from liability for a false report of child abuse; and at least some abusive parents can be rehabilitated and, if this is impossible, the child can be removed to a safer environment. As expected, the incidence of child abuse is higher in the lower socioeconomic groups where parents are often unable to handle their problems and generally have no recourse to an outside source of help. Many of these parents have themselves been beaten as children. Remedies within the competence of the physician are stressed. - *A. C. Schenker.*

2070 ***MILLER, ROBERT W.; & BLOT, WILLIAM J.** Small head size after in-utero exposure to atomic radiation. *Lancet*, 2(7781):784-787, 1972.

Examination of the data available on head circumference, intelligence, and dosimetry for 388 children in Hiroshima and 99 in Nagasaki who had been exposed to atomic bomb radiation *in utero* revealed a progressive increase with dose in the frequency of the abnormality among those whose mothers were exposed before the eighteenth week of pregnancy. When the percentages of persons with small heads in various dose groups were compared with the percentages of persons with small heads in a nonexposed control group, the Hiroshima data showed significant

($p < 0.05$) excess in the group whose mothers received as little as 10-19 rad. In Nagasaki, no effect on head circumference was observed consistently under 150+ rad. In both cities, maternal doses of 150+ rad often caused MR in association with small head circumference. Since the quality of radiation differed in the 2 cities, and a neutron influence could not be excluded for Hiroshima, the low-dose effects in this city may not be directly applicable to medical X irradiation. Effects of environmental disturbances resulting in nutritional and economic deprivation, more prevalent in Hiroshima than Nagasaki, are presumed to have been significant influences as well. (16 refs.) - *B. J. Grylack.*

2071 **SELZER, MICHAEL E.; MYERS, RONALD E.; & HOLSTEIN, STANLEY B.** Prolonged partial asphyxia: effects on fetal brain water and electrolytes. *Neurology*, 22(7):732-737, 1972.

The fetuses of 31 near-term pregnant rhesus monkeys were exposed to 3-hour episodes of liver biopsy. Operative cholangiography and wedge biopsy of the liver will establish the correct diagnosis in 98% of patients. Children with uncorrectable biliary atresia have an average life-span of 19 months. The only hope of survival in these patients is liver transplantation. (8 refs.) - *A. C. Schenker.*

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2072 **NORMAN, MARGARET G.** Antenatal neuronal loss and gliosis of the reticular formation, thalamus, and hypothalamus. A report of three cases. *Neurology*, 22(9):910-916, 1972.

Of 3 neonates seen with neuronal loss or encrustation and glial reaction in the reticular formation of the brainstem, inferior colliculus, thalamus, hypothalamus, and hippocampus, in 2 the lesions were well established at birth and were responsible for the low Apgar scores, irregularities of respiration, and absent suck and Moro reflexes noted at birth. Since the lesions in the 3 infants resembled those produced experimentally in fetal monkeys by acute asphyxia neonatorum, it was tempting to ascribe them to asphyxia. However, there was no evidence of asphyxia in the infants' history. The taking of an overdose of salicylates late in the pregnancy of the mother of 1 patient could have caused the brain damage in the child. The 3 patients died, but it is possible for infants with less severe brainstem injury occurring either before or at birth to live to form part of the population of brain-damaged children. (15 refs.) - *B. J. Grylack.*

Hospital for Sick Children
Toronto 101, Canada

2073 **CONNERS, C. KEITH.** Symposium: behavior modification by drugs. II. Psychological effects of stimulant drugs in children with minimal brain dysfunction. *Pediatrics*, 49(5):702-708, 1972.

The results of 2 studies involving administration of various psychostimulants to children with minimal brain dysfunction provide clear evidence of improved behavior and show significant drug effects on some cognitive, perceptual, and achievement measures, but they also demonstrate striking inconsistencies. In the magnesium pemoline Cylert-dextroamphetamine study, some of the most drug-sensitive measures, such as the vigilance task, did not show the effect found in the methylphenidate-dextroamphetamine (MP-DA) study, and the effects on achievement were more striking in the Cylert study. The Draw-A-Man and Bender Gestalt psychological tests showed striking and highly significant improvement in the MP-DA study but not in the Cylert study or in 2 earlier DA studies. Analysis of the results confirmed the assumption that, rather than reflecting the difference in length of treatment or dosage schedules, these differences were a function of the physiologic and psychologic heterogeneity within children with minimal brain dysfunction. - *B. J. Grylack.*

Massachusetts General Hospital
Boston, Massachusetts 02114

2074 **GESCHWIND, NORMAN.** Disorders of higher cortical function in children. *Clini-*

cal Proceedings, Children's Hospital National Medical Center, 28(10):261-272, 1972.

Insights obtained from the study of higher cortical function in adults are frequently important for the understanding of the child, and vice versa. Among the primary differences between the acquired aphasias of adulthood and childhood, the much more dramatic recovery of the child is striking. Differences also exist in the mode of recovery of the child and the adult. While the view that brain lesions in childhood produce less serious effects than those in the adult is valid in many instances, it appears at least possible that some childhood lesions may produce aphasias while the same lesions do not do so in adults. It is probably incorrect to treat all of the special learning deficits encountered in childhood as abnormalities. Gross examination of the normal brain may help to indicate the source of the remarkable variations in perceptual and learning capacities in different areas which exist in normal children. (16 refs.) - *B. J. Grylack.*

Boston City Hospital
Boston, Massachusetts 02118

2075 **DEE, HENRY L.; & VAN ALLEN, MAURICE W.** Speed of decision-making processes in patients with unilateral cerebral disease. *Archives of Neurology*, 28(3):163-166, 1973.

Decline in the speed of decision making, associated with cerebral disease, was investigated to determine whether it is a consequence of a specifically localized lesion or whether it results from a severe insult to both cerebral hemispheres. The Ss were 48 patients of whom 16 had cerebral lesions restricted to the left hemisphere, 16 had lesions in the right hemisphere, and 16 had no evidence of cerebral disease. The apparatus comprised light stimuli and response buttons which were varied as to the complexity of response required. The median reaction time for each patient under each condition served as the basic data. All groups showed a linear increase in decision making time as the number of elements involved in the decision was increased. Both groups of patients with cerebral disease showed a general increase in reaction time as compared to control patients. The major finding of the study was that left hemisphere patients show increasing impairment in mental efficiency with increasing task complexity, which is not the case with right hemisphere patients. (6 refs.) - *A. C. Schenker.*

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Iowa City, Iowa 52240

2076 **BURKINSHAW, JOHN.** Head injuries in children. *British Medical Journal*, 1(5796):378-379, 1972. (Letter)

Routine skull X-rays are not only unnecessary but may be dangerous in the management of head injuries in children, and the crucial role should be played rather by careful observation in order to detect the onset of complications, hemorrhage, and meningitis. The presence or absence of a skull fracture is not the criterion used to decide whether or not to admit a child to the hospital, and the skull X-ray is generally a wasteful and frightening procedure. - *B. J. Grylack.*

London S.E.26, England

2077 **MORTON, M. R.** Special handicaps: the overactive child. In: Griffiths, Margaret I., ed. *The Young Retarded Child: Medical Aspects of Care*. Baltimore, Maryland, Williams & Wilkins, 1973, Chapter 12, p. 134-144.

Overactivity, sometimes called hyperactivity or hyperkinesis, is a symptom not a syndrome, usually part of a multiple handicap case. The symptom is obvious, but is difficult to define, classify, or measure, and it can occur at all IQ levels. Conditions associated with overactivity include meningitis, encephalitis, MR, minor brain damage or dysfunction, epilepsy, autism, and/or sometimes family disorder. The causes of overactivity are related to cortical function, whether the disturbance be organic or psychological. Assessment of the overactive individual is a continuing process involving the child and his condition, family social history, information on pregnancy and labor, neurological examination, and clinical and school observation. Management of overactivity may include the use of drugs such as Melleril or Valium and/or alterations in the child's environment. The outcome of treatment depends upon the efficacy of diagnosis and

assistance, and may be measured in the child and in the total family environment. - *C. Wares.*

Birmingham Regional Hospital Board
Birmingham, England

2078 **EISENBERG, L.** The hyperkinetic child and stimulant drugs. *New England Journal of Medicine*, 287(5):249-250, 1972. (Editorial)

The possibility that stimulant drugs used to treat the hyperkinetic syndrome suppress growth emphasizes the need for rigorous long-term care of these patients. Despite arguments that hyperkinetic children need not be medicated at all, it has been found that children who display symptoms such as overactivity, distractibility, or aggression are at risk for academic failure, antisocial behavior, or psychopathology in early adolescence. The patients respond dramatically to the drugs, and this situation encourages doctors and parents to overlook other aspects of remedial treatment. Treatment of hyperactive children requires the simultaneous use of medication, parental guidance, educational remediation, and psychological intervention. (5 refs.) - *V. J. Goldberg.*

2079 **SAFER, D.; ALLEN, R.; & BARR, E.** Depression of growth in hyperactive children on stimulant drugs. *New England Journal of Medicine*, 287(5):217-220, 1972.

A longitudinal study of weight and height changes was done to assess the effects of prolonged administration of stimulant medication to hyperactive children. Twenty children receiving methylphenidate or dextroamphetamine had average weight gains of 0.15kg/mo during the school year. The summer weight gain of 13 children who discontinued medication during the summer was 0.45kg/mo vs the summer gain of 0.22kg/mo for the 7 who continued medication (130% and 60% of the expected weight gains, respectively). There was less weight gain suppression among children receiving less than 20mg of methylphenidate than among children receiving 10-15mg of dextroamphetamine or 30-40mg methylphenidate. Nine children who received stimulant drugs for 2 or more yr gained an average of 1.8kg/yr vs the expected 3.1kg/yr, and the deviation from the expected weight gain was significant in 8 of 9 cases. The percentile height decreased in 5 of 9 chronically medicated children, and the differences between the rates of height and weight changes among the medicated children and 7 unmedicated hyperactive children were significantly different. The effect of stimulant drugs on weight gain may be secondary to central appetite suppression. Because of the effects of prolonged use of stimulant drugs on growth, low doses of methylphenidate should be used where possible and the drug discontinued on weekends and school holidays. (18 refs.) - *V. J. Goldberg.*

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2080 **SANDERS, WYMAN R.** Resistance to dealing with parents of battered children. *Pediatrics*, 50(6):853-857, 1972.

The problem of dealing with parents of the battered child is discussed from the viewpoint of the caretaking person and the type of abuse which is reportable. It is understandable that a physician, nurse, or social worker would want to be certain of the facts before making a report to the authorities, but it is often difficult to obtain sufficient data to make an accurate judgment. It is suggested that a purely factual statement be made in which the caretaking person express his opinion that the child was abused and that for this reason the report must be made. In a hospital, the actual report may be made in collaboration with an experienced member of the ward or with an emergency room team. When the reporting person is able to deal with his own feelings, he is in a better position to understand that the parents as well as the child are in need of help. He can then offer this help in a supportive and acceptable way. (15 refs.) - *A. C. Schenker.*

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Los Angeles, California 90024

2081 Maltreatment of children: the battered child syndrome. *Pediatrics*, 50(1):160-161, 1972.

The Committee on Infant and Preschool Child

has issued a statement concerning the problem of the battered child. The Committee reaffirms and supports some of the recommendations of the 1966 report: that physicians continue to be required to report suspected instances, that the responsible agency receiving the report have adequate personnel and resources to take immediate action, that reported cases be evaluated promptly and appropriate service be provided for child and family, that the child be protected by the agency, that a central register of all such cases be maintained, and that the reporting physician or hospital be granted immunity from suit. Added to these recommendations, it is recommended that: valid predictive questionnaires be used in identifying parents with potential for abuse, crisis management programs be developed, child abuse diagnostic and/or treatment centers be established, increased responsibility by physicians and hospitals be encouraged, and day care services be utilized whenever appropriate. (10 refs.) - *A. C. Schenker.*

2082 MITCHELL, DOROTHY E.; & ADAMS, J. HUME. Primary focal impact damage to the brainstem in blunt head injuries. Does it exist? *Lancet*, 2(7823):215-218, 1973.

In a histologic analysis of the nature and distribution of abnormalities in serial blocks of brainstem from a consecutive series of 150 fatal, blunt (nonmissile) head injuries, 7 of the 18 Ss without histologic evidence of raised intracranial pressure had damage in the brainstem that could be attributed only to the head injury. All 7 had focal abnormalities in the region of 1 or both superior cerebellar peduncles as well as an abnormality in the corpus callosum, and the 5 cases who survived for longer than 8 days showed microglial stars or degeneration of myelin in the cerebral hemispheres. Each patient had been unconscious from the time of impact until death. The data suggested that what is referred to as the syndrome of primary brainstem damage is more accurately described as the manifestations of brainstem dysfunction occurring soon after injury. (13 refs.) - *B. J. Grylack.*

Institute of Neurological Sciences
Southern General Hospital
Glasgow G51 4TF, Scotland

2083 COLCLOUGH, I. R. Victorian Government's Report on Child Abuse: a re-investigation. *Medical Journal of Australia*, 2(27):1491-1497, 1972.

The results of an official report of the Victorian government and a student elective survey with regard to child abuse are conflicting. The Victorian Government Committee, established in 1967 to investigate allegations of child maltreatment in Victoria, reported few if any serious cases of abuse at the hospitals contacted. However, the efforts of the Committee were hindered by lack of cooperation on the part of 1 hospital and several medical superintendents. Thus, not all child abuse cases could be located. In contrast, the student survey, which involved 16 hospitals, including 7 contacted by the Government Committee, located 26 cases of maltreatment. The present system of voluntary reporting of child abuse cases is unsatisfactory and should be improved by the passage of needed legislation. (8 refs.) - *B. J. Grylack.*

2084 BERGGREEN, SHEILA MARGARET. Accidents and surgical emergencies in a population of mentally retarded children. *Acta Paediatrica Scandinavica*, 62(3):289-296, 1973.

A pilot study undertaken to review and investigate retrospectively the casualties and surgical emergencies occurring during a 3-year period in a children's hospital in Denmark for MRs revealed a total of 408 injuries among approximately 300 patients, an incidence about 3 times as high as that in the normal Danish population. The maximum number of accidents (12.5% of the total) occurred in a ward for teenage children suffering from severe epilepsy. A ward for PMR and SMR children, among them some mongols, and another ward for teenagers, several of whom are epileptics, each accounted for 8% of the total number. Injuries of the head and face constituted 42% of all injuries, injuries to the upper limbs 22%, injuries to the lower limbs 19%, and burns slightly over 4%. Because of the delayed motor and mental development of these children, accidents which occur normally among toddlers occur here in a considerably older age group and with more serious consequences, since the children are heavier and more clumsy. Where severe epileptics and spastics are concerned, the environment must be adapted to their needs. Only when ideal surroundings have been achieved can max-

imum activity be encouraged and overprotection avoided. (12 refs.) - *B. J. Grylack.*

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2085 WEINER, MICHAEL J. Hospital admission after head injury. *Lancet,* 2(7825): 382, 1973. (Letter)

Hospital admission following head trauma should be determined by symptoms and physical findings suggestive of serious injury. Studies have shown that radiographic skull examination for various instances of head trauma yields a very low percentage of skull fractures in terms of total numbers of examinations. Moreover, the detection, location, and type of fractures appear to have no correlation with the symptoms and physical findings. Clinical findings should be the determinant of treatment. (4 refs.) - *B. J. Grylack.*

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2086 OLNEY, JOHN W.; SHARPE, LAWRENCE G.; & FEIGIN, RALPH D. Glutamate-induced brain damage in infant primates. *Journal of Neuropathology and Experimental Neurology,* 31(3):464-488, 1972.

Evidence for a neuron-necrotizing process was found in the hypothalamus of each of 6 infant rhesus monkeys treated with monosodium L-glutamate (MSG) and in none of 3 NaCl-treated controls. Infants receiving relatively low oral doses of MSG (1 and 2g/kg) sustained small focal lesions confined primarily to the rostroventral aspect of the infundibular nucleus, while infants given high subcutaneous doses developed lesions which spread throughout and sometimes beyond the infundibular nucleus. Necrosis of neurons within 5 hours was a unique characteristic of the MSG-induced reaction pattern at all doses tested (1-4g/kg) and by oral and subcutaneous administration. Although the data suggested that a blood glutamate concentration of 20mg% is the threshold value for occurrence of brain lesions in the average normal primate infant, some individuals might be resistant to damage from blood glutamate levels in this range. The data did not support the view that subprimates alone are susceptible to MSG-induced neurotoxicity, since the lesions in some primates following relatively high subcutaneous doses of MSG closely resembled those observed consistently in mice treated with high doses of MSG. A causal link between low oral doses of MSG and necrosis of neurons in the infant primate hypothalamus also seemed likely. (41 refs.) - *B. J. Grylack.*

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2087 NICHAMIN, SAMUEL J. Recognizing minimal cerebral dysfunction in the infant and toddler. *Clinical Pediatrics,* 11(5):255-257, 1972.

Certain early behavioral signs in the infant and toddler should alert the experienced pediatrician to the possible existence of minimal cerebral dysfunction. Included in this profile is atypical infant behavior, characterized either by extreme lethargy or hyperactivity. Language development is often delayed, and their impulsive driven activity as toddlers makes these children accident-prone and given to violent temper tantrums. During this period, as well, intensely deviant behavior may be interspersed with practically normal behavior, making an experienced evaluation of the quality and degree of the aberrant behavior essential to an accurate clinical impression of probable minimal brain dysfunction. Until the actual diagnosis is confirmed, however, parents probably ought not to be informed directly to avoid undue guilt and despair. Where hyperactivity and deviant behavior are excessive, methylphenidate in small doses may be prescribed to help alleviate the inevitable family tensions. (5 refs.) - *N. Mize.*

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2088 CLEMMENS, RAYMOND; & KENNY, THOMAS J. Clinical correlates of learning disabilities, minimal brain dysfunction and hyperactivity. *Clinical Pediatrics,* 11(6):311-313, 1972.

The wide range of clinical conditions encom-

passed by the terms learning disability, minimal brain dysfunction, and hyperactivity only underscores the imprecise and subjective nature of the neurological diagnosis in children. Nowhere are the limitations of existing diagnostic tools more obvious than in the evaluation of children suspected of having a learning disability. During 13 years of clinical experience, it has become obvious to us that, among other things, the separation of mind and body is an artificial and harmful dichotomy, that the definition of "normal" behavior must be constantly reassessed, and that educational and remediation techniques are more appropriate for hyperactive children than are medical and neurological procedures. Overall, the diagnosis and treatment of the atypical child demands a collective approach, one involving both physicians and educators in all aspects of the child's maturation. (7 res.) - *N. Mize.*

University of Maryland School of Medicine
Baltimore, Maryland 21201

2089 **ISSACS, SUSANNA.** Neglect, cruelty, and battering. *British Medical Journal,* 3(7):224-226, 1972.

The growing body of knowledge concerning child abuse offers definitive evidence that a great portion of the inflicted damage can be prevented. The handling of potential cases of child abuse demands a sympathetic and concerned outlook with controlled curiosity, not a suspicious oversimplified view rooted in rhetoric. Diagnostic clues which may be useful as indicators of abuse include contradictory and implausible explanations for child injuries and strong contrast between parental attention to child grooming and concern for weight gain. Extreme defensive sensitivity may also alert the attending physician of unusual circumstances. Often the demeanor taken by "battering parents" is that of shock insulating ignorance. In any event, the "battered baby syndrome" may have its origins in emotionally and/or physically abused rearing of the parents. A personality disorder of the parent in early childhood may leave an individual unsure of his worth, very vulnerable to the opinions of others, and highly dependent on external proof that all is well. In the light of such parental sensitivity, the use of questionnaires or any form of official approach may be self defeating since the feeling of being dehumanized can easily arise. Generally unless there is parental psychosis present, there is little great risk to siblings of injured children. The experience of the author shows a general cooperation among parents who are referred to further psychiatric care. Emphasis on the criminology, punitive aspects, and incarceration can be of great potential harm to disordered parents. Fortunately, most parents referred to psychiatric units do not require constant interpretative psychotherapy, a need which could severely tax psychiatric personnel resources. (7 refs.) - *K. Der.*

Paddington Green Children's Hospital
London, England

2090 **SHETTY, TARANATH.** Alpha rhythms in the hyperkinetic child. *Nature,* 238(5358):43-44, 1972.

Additional clarification of previously reported research on alpha rhythms in the hyperkinetic child is presented. The magnetic tape recordings from which *r* values of Table 1 were computed were obtained under two different filter settings. Eight EEG's (6 patients, 2 controls) were recorded on f.m. tape with 10 cycle low pass filter and 9 (6 patients, 3 controls) were recorded with 1 cycle filter. Data from 12 Ss and all 5 controls were collected directly on f.m. tape; data from 16 Ss were transferred to f.m. tape from ink writing charts. Because of high paper speed to the reader, attenuation of high frequency components of the EEG existed in this group. The alpha band was least affected by these maneuvers; this band was also found to be the most sensitive. The compilation of data should be considered preliminary because of these limitations. (1 ref.) - *A. C. Schenker.*

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Boston, Massachusetts 02115

2091 **MANN, LEON I.; CARMICHAEL, ANDREW; & DUCHIN, SYBIL.** The effect of head compression on FHR, brain metabolism and function. *Obstetrics and Gynecology,* 39(5):721-726, 1972.

Sufficient force, mimicking uterine contractions, was applied to 15 fetal lambs until changes in the fetal EEG were observed. Head compression

was correlated with increases in perfusion pressure and vascular resistance and with decreases in blood flow and oxygen consumption. These findings support the hypothesis that changes in fetal heart rate and EEG are attributable to transient episodes of cerebral ischemia and suggest that the higher incidence of MR and motor abnormalities observed in children born after prolonged labor may be due to injuries sustained during prolonged head compression. (15 refs.) - *V. J. Goldberg.*

Cornell Medical Center
New York, New York 10021

2092 McNAMARA, JOHN J. Hyperactivity in the apartment bound child. *Clinical Pediatrics*, 11(7):371-372, July 1972.

Increasingly, numbers of children living in high density urban slums, like the South Bronx, are exhibiting a distinctive "hyperactive" behavior pattern. In school and during non-TV hours at home, these children become hyperactive. Parents tend to keep their children indoors constantly, fearing for their safety when left to play in the teeming streets, and the children respond to this curtailment of their physical energy by becoming "hyperactive." Adequate physical outlets in a safe setting, such as provided by parks and other recreational facilities, are the remedy. (5 refs.) - *N. Mize.*

Lincoln Hospital
Bronx, New York 10454

2093 HOWELL, MARY C.; REVER, GEORGE W.; SCHOLL, MARY L.; TROWBRIDGE, FREDERICK; & RUTLEDGE, ANNE. Hyperactivity in children. *Clinical Pediatrics*, 11(1):30-39, January 1972.

Over the years, the scientific understanding of hyperactivity in children has undergone many transformations. Different investigators have tended to emphasize different characteristics of the syndrome, with resulting differences in the identified types, diagnosis, drug therapy, and approaches to management. The case history of an 11-yer-old hyperactive black girl illustrates one possible program of management in which the home and family environment were carefully considered by a team of specialists. The child's excitability, tantrums, aggressiveness, and erratic school performance were all improved when Ritalin was administered regularly. Generally, drug treatment is most effective in instances of primary hyperactivity, such as in the case cited. Primary hyperactivity is characterized by excessive activity attributable to a high energy level, motor incoordination, or perceptual distractibility. Secondary hyperactivity, on the other hand, is simply a symptom of or reaction to a more basic problem and will usually not respond to drug therapy alone. (14 refs.) - *N. Mize.*

Massachusetts General Hospital
Boston, Massachusetts

2094 SHELLEY, EDWARD M.; & *REISTER, ALBERT. Syndrome of minimal brain damage in young adults. *Diseases of the Nervous System*, 33(5):335-338, 1972.

Sixteen 18- to 23-yr-olds (14 males) were found unable to cope with the "basic tasks" of military training. Psychiatric interviews revealed that each had long been considered sloppy or clumsy and had learned to compensate for these deficits, but military training which required a high degree of visual-motor competency unmasked their deficiencies. No gross neurological abnormalities were found, but manifest soft signs included clumsiness in 12 of 16, poor balance in 7, confused laterality in 7, disturbed coordination in 6, poor fine finger activity or dysdiadochokinesia in 5, and speech disturbance in 3. The WAIS results were verbal, 105.8; performance, 83.8; and full test, 96.1. On the Bender-Gestalt designs, the Ss made errors and had great difficulty with figures A and 7, the designs most frequently distorted by neurologically dysfunctioning patients. The child development questionnaires reported 14 of 16 with temper tantrums, 12 with hyperkinetic behavior syndrome (which disappeared at the onset of puberty), 12 with early difficulties in school performance, and 10 with speech problems. These patients retained perceptual-motor defects which precluded optimal military performance. (6 refs.) - *V. J. Goldberg.*

*2135 Babcock Road
San Antonio, Texas 78229

2095 NATELSON, STEPHEN E.; & SAYERS, MARTIN P. The fate of children sus-

taining severe head trauma during birth. *Pediatrics*, 51(2):169-174, 1973.

A follow-up of 42 children with neonatal brain injury was carried out over a 5-year period; all of these patients had some type of grossly recognizable trauma. The study was carried out (from data obtained from physicians or hospitals) in children who had sustained this injury from 8 to 13 years previously; there were 27 boys and 15 girls. Six of the 42 children (14%) died within a week after admission; 5 cases suffered acute subdural hematoma after breech delivery, difficult high forceps, or a premature separation of the placenta resulting in a hasty delivery with forceps. Five of these infants also had congenital abnormalities. There were 13 children with chronic subdural hematoma, 11 of whom presented with seizures and 2 others who developed these in the hospital; multiple subdural taps were successful in 4; 2 children are normal at 7 and 12 years of age, and a third is doing average work at 11. Of 9 children subjected to neonatal stripping, 4 had bilateral hematomas. Of the 15 infants who had closed, depressed skull fractures, 13 are now normal. The morbidity of chronic subdural hematoma was nearly 80%. The overall results of the follow-up were: 31% normal; 14% mildly handicapped; 43% had died, and 12% could not be located. (16 refs.) - *A. C. Schenker.*

307 Fort Sanders Professional Building
Knoxville, Tennessee 37916

2096 **BROWN, A. W.; & BRIERLEY, J. B.** Anoxic-ischaemic cell change in rat brain: light microscopic and fine-structural observations. *Journal of the Neurological Sciences*, 16(1):59-84, 1972.

Anoxic-ischemic neuronal changes were observed in rats, by combined light and electron microscopy, for the effect of intermittent exposure to nitrogen, with and without interruption of blood flow in the right common carotid artery. The Ss were adult female white Wistar rats; 7 animals were exposed to nitrogen after application of the artery clasp. When apnea occurred the animals were artificially ventilated until spontaneous respiration resumed; quiescence in gas flow, hyperpnea, convulsion, apnea, and mechanical ventilation were repeated (4-17 times) during 40 min exposure. Two normal rats were also exposed to nitrogen for 40 min. All animals were observed for survival. Controls consisted of 4 normal rats and 2 in which the artery clasp had been applied for 2.5 hours. The animals were killed by perfusion fixation with glutaraldehyde after survivals of 45 min-2 hr. Microvacuolation and ischemic cell change were observed in the neocortex and hippocampus of both groups of animals. The majority of microvacuoles in the neuronal cytoplasm corresponded to swollen mitochondria, with dilatations of both smooth and granular endoplasmic reticulum, and an apparent increase in ribosomes and in cytoplasmic matrix density. Ischemic cell change appeared to occur by progressive condensation of the cytoplasm between intraneuronal spaces. Swollen astrocytic processes were prevalent. (35 refs.) - *A. C. Schenker.*

Medical Research Council
Neuropsychiatric Unit
Carshalton, Surrey, Great Britain

2097 **NEWBERGER, ELI H.; HAGENBUCH, JOHN J.; EBELING, NANCY B.; COLLIGAN, ELIZABETH PIVCHIK; SHEEHAN, JANE S.; & MCVEIGH, SUSAN H.** Reducing the literal and human cost of child abuse: impact of a new hospital management system. *Pediatrics*, 51(5):840-848, 1973.

An attempt to demonstrate the effectiveness of a collaborative community effort to provide preventive and therapeutic help to victims of child abuse and their families is described. A shortage of personnel in the state agency designated to deal with child abuse reports led to an appraisal of the prevailing hospital case management. This resulted in the formation of a group of interested individuals who reviewed the problem and proposed the integration of 3 agencies into a consultation group in association with the Children's Hospital. This group, the Trauma X group, was shown to reduce the costs of medical service and the risk of reinjury subsequent to the diagnosis of child abuse. This was due to the availability of follow-up information once the program of regular surveillance began. The data presented suggest that a hospital can serve as an effective portal of entry into the child health and welfare service system for disorganized families whose children's lives are in jeopardy. (11 refs.) - *A. C. Schenker.*

The Children's Hospital Medical Center
Boston, Massachusetts 02115

2098 **SAFER, DANIEL J.; & ALLEN, RICHARD P.** Factors influencing the suppressant effects of two stimulant drugs on the growth of hyperactive children. *Pediatrics*, 51(4):660-667, 1973.

The prolonged use of stimulant drugs in hyperactive children was studied for their effects on the growth in weight and height. The Ss comprised 29 children on dextroamphetamine sulfate, 20 children on methylphenidate, and 14 hyperactive children who had not received any drugs. The results revealed that the suppressant effects of stimulant drugs on the weight gain of hyperactive children persist beyond the initial period of medication; long-term use of stimulant medication causes an inhibition of growth in height which is proportional to the weight suppression; the suppression of growth caused by dextroamphetamine is significantly greater than that caused by methylphenidate; and the growth suppressant effects of methylphenidate are notable only for daily doses over 20mg. Some patients may respond to one stimulant and not to another; dextroamphetamine is recommended for use in hyperactive children from ages 3 to 6 years. (12 refs.) - *A. C. Schenker.*

Baltimore County Department of Health
Baltimore, Maryland 21221

2099 **KEMPE, C. HENRY.** A practical approach to the protection of the abused child and rehabilitation of the abusing parent. *Pediatrics*, 51(4):804-812, 1973.

The concept that many parents do not have the qualities required for the care of their children is developed and a rational approach to child protection is discussed. The clinical approach to child abuse problems starts with prediction. In Denver, the factors leading to child abuse have been studied, and questionnaires have been developed which are applied prenatally. A study is being conducted in Aberdeen, Scotland, in which 65 nurses visit every house with a new baby and observe the mother and child. Battering parents are very defensive about being criticized and don't like to be watched. Every child who has an accident or who fails to thrive is then studied; questionnaires are answered very differently by abusing parents than by protective parents. It is recommended that when major injury occurs all reported cases should lead to court filing. There should be accurate psychiatric diagnosis of family abnormality made in every child abuse case. There are many families who are willing to adopt children who are unwanted by their parents, or to offer foster care to such children. Parental rights should be terminated where parenting will never occur. - *A. C. Schenker.*

University of Colorado School of Medicine
Denver, Colorado

2100 **KELLEY, FLORENCE M.** Role of the courts. *Pediatrics*, 51 (4, Part II):796-798, 1973.

The role of the court in the area of abused and neglected children is defined. The Family Court is dependent on evidence which must conform to strict rules before action is taken; when presented with controversial evidence on behalf of both the child and the parents, the judge must weigh the evidence and make the decision. However, even when the judge decides that the parent has deliberately injured the child, the Family Court has no authority to punish the parent. The court can remove the child or the parent from the household, but cannot punish. A court, within its restrictions, may not be as responsive as a facility without restrictions. In any case, the power of punishment of the parents does not ultimately help the child. Such help can possibly be found in the community without legal procedure. In terms of human behavior, dealing directly with the parents offers more hope for the child than does litigation. The judge is not trained in this field of competence and is moreover restricted by court ruling. - *A. C. Schenker.*

Family Court of the State of New York
New York City, New York

2101 **HELFER, RAY M.** The etiology of child abuse. *Pediatrics*, 51(4, Part II), 1973.

The etiology of child abuse is analyzed in terms of the components: potential for abuse, the kind of child, and a crisis or a series of crises. The potential for abuse often harks back to the way the parents themselves were reared. Another element of such potential may be the incapacity of the parents, the mother in particular, to turn to someone else for help in a tense situation. The relationship between the parents is an important

component of this potential, whether they can relieve each other in a time of stress. Parents who abuse children usually expect the child to do something for them. The child who is the victim of abuse is usually different from the rest of the children, or he may be perceived as different. Sometimes he may have a birth defect or be hyperactive. A crisis, or series of crises, may precipitate the abuse in a home where the other components are present. Solving the crisis alone is not enough to prevent child abuse in the future in such surroundings. - *A. C. Schenker.*

College of Human Medicine
Michigan State University
East Lansing, Michigan

2102 FONTANA, VINCENT J. The diagnosis of the maltreatment syndrome in children. *Pediatrics*, 51(4, Part II):780-782, 1973.

The recognition of symptoms of maltreatment of children is delineated for the benefit of all mandated sources under the present child abuse law, especially the physician in the hospital. The neglect and abuse of children denotes a situation ranging from the deprivation of food, clothing, shelter, and parental love to physical abuse and mistreatment. The maltreated child is often brought to the physician or hospital with a history of failure to thrive, repressed personality, or irritability. The severely abused children usually appear in emergency clinics with external evidence of trauma, and sometimes in a state of coma, convulsions, or even death. A table of the physician's index of suspicion is presented which relates to the history, physical examination, differential diagnosis, and radiologic manifestations. In addition to his diagnosis, a social service investigation will confirm the diagnosis of maltreatment. The child's appearance often tells a story of neglect, and the parental attitudes may also justify suspicion. - *A. C. Schenker.*

St. Vincent's Hospital
New York, New York

2103 JOYNER, EDMUND N. Child abuse: the role of the physician and the hospital (symposium). *Pediatrics*, 51(4, Part II):799-803, 1973.

The responsibilities of the physician and of the hospital in the protection of the child against abuse are discussed. The basic fault of the medical profession lies in the failure to educate its practitioners concerning the prevalence of child abuse. The physician should be aware of the symptomatology of such abuse and carry out his mandated responsibilities for the protection of the child. The role of the hospital is that of recognition, protection, healing of bodily and emotional injuries, fulfilling of mandated reporting procedures, and treatment, and if possible, rehabilitation of abusing parents. The hospital must develop intramural educational programs for the benefit of its personnel to recognize the symptoms of child abuse. Under present conditions, the hospital must take on the role of making the home safe through rehabilitation of the parents, a role for which no other agency is available. This role can best be fulfilled through an interdisciplinary team and requires the added support of legislature. - *A. C. Schenker.*

Roosevelt Hospital
New York City, New York

2104 ISSACS, JACOB L. The law and the abused and neglected child. *Pediatrics*, 51(4, Part II):783-792, 1973.

Laws regarding protective proceedings in the Family Court are discussed. In New York, any practitioner, teacher, or other professional person who suspects that a child under 16 years of age has been subject to physical injury or other form of abuse other than by accidental means is required to report to the City Department of Social Services. Legislation passed in 1969 and 1970 authorized any hospital which has in its charge a child suspected of being abused, to hold that child in custody until the next regular workday session of that part of the Family Court which is charged with processing such cases. Neither the physician-patient privilege nor the privilege attaching confidential communications between husband and wife are grounds for excluding evidence regarding child abuse. The law is flexible with respect to disposition of the case, dependent upon the extent of child abuse. It is also recognized that rehabilitative treatment may produce changes over a period of time which permit the child to be returned home, after he had been removed for a certain interval. The law provides for subsequent rehearing and application to the court for a change of disposition when circumstances require it. - *A. C. Schenker.*

2105 **CAMERON, JAMES S.** Role of the child protective organization. *Pediatrics*, 51(4, Part II):793-795, 1973.

Protective services on behalf of neglected and abused children in New York are described. The Public Social Service Department is obliged to initiate and provide services whenever there is a complaint that a child's wellbeing is jeopardized. The report to this department is not designed to set into motion punitive actions against the parent, but is a first step in ensuring the child's immediate and future wellbeing by providing help to the child and his family. Protective Services carry the responsibility for invoking the authority of the court to secure adequate protection, care, and treatment of children whose parents are unable or unwilling to use the help available to them. The responsibility for effective coordination between the Protective Service Agency and other resources rests with the Protective Services worker. The mandate to protect a child also provides the responsibility to safeguard his welfare and to preserve and stabilize his family whenever possible. - *A. C. Schenker.*

2106 **ANTOON, ALIA Y.; VOLPE, JOSEPH J.; & CRAWFORD, JOHN D.** Burn encephalopathy in children. *Pediatrics*, 50(4):609-616, 1972.

A survey of burn encephalopathy among 140 children with acute thermal injuries hospitalized during a 2-year period indicated that burn encephalopathy in children almost invariably has an easily definable cause and, with appropriate treatment, a favorable prognosis. Of the 20 patients who manifested neurological disturbances, the etiology of the neurological syndome was defined readily in 19. Mortality was high (50%), but all except 1 survivor showed complete neurological recovery. Only 1 death was due primarily to the central nervous system insult, the others resulting from uncontrolled infections. Hypoxia was the main determinant in 9 of the 20 cases, hypovolemia in 1, sepsis in 4, hyponatremia in 4, and cortical vein thrombosis caused focal seizures in 1. (20 refs.) - *B. J. Grylack.*

Shriners Burns Institute
50 Blossom Street
Boston, Massachusetts 02114

MEDICAL ASPECTS—Diseases or disorders of metabolism and growth

2107 **FERRO-LUZZI, G.** Protein/calorie malnutrition. *Lancet*, 2(7780):769, 1972. (Letter)

Protein deficiency without an associated total energy lack is uncommon in areas where infants are weaned on cereal paps, whereas cases of severe protein/calorie malnutrition, associated with total energy lack, are quite common in such localities. Cases of protein/calorie malnutrition observed in Eritrea (Ethiopia) were labelled *Mehlnahrschaden*, not kwashiorkor, since the staple foods of this population are millets relatively high in protein. Cases of kwashiorkor require proteins, whereas cases of *Mehlnahrschaden* demand a better use of available proteins or an improvement in the hygienic milieu of the child. - *B. J. Grylack.*

Via Mario Fascetti, 67
00136-Rome, Italy

2108 **TURNER, R. C.; SPATHIS, G. S.; NABARRO, J. D. N.; & DORMANDY, T. L.** Familial fructose and galactose intolerance. *Lancet*, 2(7782):872, 1972.

The propositus and only surviving affected member of a family with reported familial fructose and galactose intolerance was investigated. Initial study had revealed hypoglycemia induced by fructose or galactose, a very high fasting plasma insulin level, and an excessive insulin response to glucose. After 10 years on a high-glucose, low-fructose, and low-galactose diet punctuated by convulsant attacks relieved by glucose, a recent hospitalization failed to demonstrate any type of hypoglycemia, and plasma insulin levels and responses were normal. Previous results could not be correlated satisfactorily with the present findings. (2 refs.) - *B. J. Grylack.*

Middlesex Hospital Medical School
London W.1, England

2109 **BEARN, ALEXANDER G.** Cell culture in

inherited disease—with some notes on genetic heterogeneity. *New England Journal of Medicine,* 286(14):764-767, 1972.

Study of cultured skin cells has made it possible to identify many inherited metabolic diseases by detecting specific biochemical consequences of gene activity *in vitro.* Tissue cultures may reveal a marked deficiency of a specific enzyme activity in homozygous mutant cells and a 50% decrease in cells heterozygous for the mutant gene. (Immunologic or other methods must be used to determine specific protein concentration.) Possibility of deep-freezing the cultured cells is important in the case of extremely rare diseases such as orotic aciduria. Inherited enzyme defects now detectable in fibroblast cultures include acatalasia, citrullinemia, Lesch-Nyhan syndrome, and the lysosomal diseases. Application of tissue culture to inherited disease has also revealed the existence of genetic heterogeneity, which is indicated (nonspecifically) through cellular metachromasia for many conditions. In the mucopolysaccharidoses, where the primary defect leads probably to a decrease in mucopolysaccharide cellular degradation and subsequently to the accumulation of this substance within the cells and concomitant organ dysfunction, human serum or normal cell tissue culture fluid can be added to the tissue culture to achieve a marked decrease in the excess intracellular mucopolysaccharide. Such a factor can be used to investigate genetic heterogeneity among the mucopolysaccharidoses. The greater the extent of genetic heterogeneity, the more excessive are present estimates of human mutation rates for specific diseases. (10 refs.) - *N. Jarvis.*

New York Hospital—Cornell Medical Center
New York, New York 10021

2110 **GOMEZ, MANUEL R.; ENGEL, ANDREW G.; & DYCK, PETER J.** Progressive ataxia, retinal degeneration, neuromyopathy, and mental subnormality in a patient with true hypoparathyroidism, dwarfism, malabsorption, and cholelithiasis. *Neurology,* 22(8):849-855, 1972.

A 25-year-old woman had a rare association of signs and symptoms implicating the central and peripheral nervous systems, skeletal muscle, parathyroid glands, and the gastrointestinal tract. Some features of her illness were consistent with known neuromuscular disturbances, but primary hypoparathyroidism seemed to be unique to this patient. While the primary metabolic abnormality might have been directly responsible for each of the observed somatic features of the syndrome in the woman, malabsorption alone could account for the dwarfism, peripheral neuropathy, and myopathy, and some of the patient's ataxia could be secondary to the peripheral neuropathy. The biochemical defect in the case remains to be determined. (9 refs.) - *B. J. Grylack.*

Mayo Clinic
Rochester, Minnesota 55901

2111 **RAINE, D. N.; COOKE, J. R.; ANDREWS, W. A.; & MAHON, D. F.** Screening for inherited metabolic disease by plasma chromatography (Scriver) in a large city. *British Medical Journal,* 3(5817):7-13, 1972.

The Scriver plasma chromatography screen for inherited metabolic disease was initiated in Birmingham, England. Collections of capillary blood were made by midwives on domiciliary service or came from 2 large maternity hospitals. The test demonstrated a potential for detecting abnormalities of phenylalanine, histidine, proline, hyperlipidemia, tyrosinemia, methionine, branched-chain amino acids, and certain other metabolic defects. Analysis of the specific diagnoses made during 3 years of testing all neonates in Birmingham showed, however, that there could be a considerable delay in confirming a suspected diagnosis and that the significance of a particular and apparently specific chemical abnormality in the neonatal period was not always well established. Repeated testing was required frequently, either because of technical failures or an abnormal chromatographic pattern. The organization of effective methods for delivery and collection of specimens and for interpretation of chromatograms also presented problems. (27 refs.) - *B. J. Grylack.*

Children's Hospital
Birmingham 16, England

2112 **DANES, B. SHANNON; DEGNAN, MARK; SALK, LEE; & FLYNN, FREDERICK J.** Treatment of Hurler

syndrome. *Lancet*, 2(7782):883, 1972. (Letter)

Experience with a child with Hurler syndrome has emphasized the need for critical evaluation of plasma infusions for the mucopolysaccharidoses. A program of weekly infusions of fresh, frozen plasma was instituted when the infant was 2 months old in order to determine the efficacy of such plasma in modifying the course of the Hurler syndrome. The urinary mucopolysaccharide degradation ratio was used to monitor alterations in mucopolysaccharide metabolism. The affected older sibling maintained a 0.4 ratio, whereas the patient maintained a ratio of 1.0 to 2.0 during 16 months of weekly plasma infusions. There was no significant change in the total amount or ratio of large molecular weight mucopolysaccharides to fragments in the urine during weekly infusions. At 18 months of age, the infant manifests all of the characteristic physical changes of a child with Hurler syndrome, is functioning at the 12-month level of psychomotor development, and has received a ventriculoatrial shunt for hydrocephalus. (1 ref.) - *B. J. Grylack.*

New York Hospital
Cornell Medical Center
New York, New York 10021

2113 **FOX, JACOB H.; FISHMAN, MARVIN A.; DODGE, PHILIP R.; & PRENSKY, ARTHUR L.** The effect of malnutrition on human central nervous system myelin. *Neurology*, 22(12):1213-1216, 1972.

A study was done of myelin isolated from the white matter of 3 malnourished infants and 3 control infants. No significant differences in the composition of the myelin from the brains of the 2 groups were detected. The finding of normal composition of the myelin from malnourished human brains indicated that the low content of white matter lipids noted previously was probably due to a decreased amount of chemically normal myelin rather than to an alteration in the composition of the membrane. The finding of a reduced amount of normal myelin suggests that the most deleterious effect of undernutrition may be on those events preceding myelination in the nervous system. (22 refs.) - *B. J. Grylack.*

Washington University School of Medicine
St. Louis, Missouri

2114 Consequences of malnutrition. *Canadian Medical Association Journal*, 106:849, 1972. (Editorial)

Research on the effects of mild to moderate protein-calorie malnutrition on children indicates that the child recovered from serious malnutrition may be unharmed. Evidence has shown that while classical kwashiorkor leads to a failure of adaptation, possibly because of the inhibitory effects of dietary carbohydrate on tissue catabolism, marasmus represents effective metabolic adaptation carried to pathological limits. A Cape Town (South Africa) research team recently reported no significant differences in intelligence scores between mixed race kwashiorkor children at the tenth year of follow-up who had been hospitalized in infancy and their healthy siblings. The significantly lower scores achieved by the late onset kwashiorkor group in a drawing test and a problems subtest in comparison with their early onset counterparts were contrary to expectations. A second paper dealing with larger groups followed up for 10 years concluded that no case of malnutrition should be regarded as beyond help, a finding that is consistent with the results of a discussion on intellectual development after malnutrition held at the World Congress of Psychiatry in Mexico City (December 1971). - *B. J. Grylack.*

2115 **KUMAR, VIJAY; CHASE, H. PETER; HAMMOND, KEITH; & O'BRIEN, DONOUGH.** Alterations in blood biochemical tests in progressive protein malnutrition. *Pediatrics*, 49(5):736-743, 1972.

Alterations in blood biochemical parameters resulting from progressive protein deprivation were studied longitudinally in 8 young female pigtail monkeys (Macaca nemestrina), known to develop a condition similar to human kwashiorkor following protein deprivation. These animals were fed synthetic standard monkey diet (SKF), 4 control animals were fed the standard 35% protein SKF diet, and 4 other control animals received a synthetic isocaloric, no-protein diet. Body weights in the protein-deprived monkeys declined progressively, with statistically significant differences ($p<.05$) noted after 10 weeks of

protein-free diets, and poorly nourished animals developed facial edema after 15 weeks. Protein deprivation of between 2 and 12 weeks' duration resulted in significant acute decreases in hematocrits, serum urea nitrogen levels, and amylase activity ($p<.05$) and in progressive reduction in serum total proteins, albumin levels, and transferrin. Five of the 7 measured essential amino acids showed statistically significant ($p<.05$) reductions in serum concentration after 8 or 14 weeks of low-protein diet. Of the nonessential amino acids, tyrosine, arginine, and glutamic acid also showed statistically significant decreases ($p<.05$). (27 refs.) - *B. J. Grylack.*

University of Colorado Medical Center
Denver, Colorado 80220

2116 Committee on Children with Handicaps. Phenylketonuria and the phenylalaninemias of infancy. *Pediatrics*, 49(4):628-629, 1972.

In light of gaps in knowledge at the time of the 1965 statement of the Committee on Children with Handicaps outlining the responsibilities of the physician to the child with phenylketonuria, a new statement reflecting recently acquired information about the disorder has been issued. An increased phenylalanine level in the blood can occur in the absence of disease but is always present in phenylketonuria. Screening programs are the best available means for identifying infants with protein metabolism abnormalities resulting in serum phenylalanine elevations. Different approaches seem indicated for the management of the disorder. The Committee recommends that, whenever feasible, a child with phenylketonuria should be followed routinely in a clinic or university setting by specialists in the field. - *B. J. Grylack.*

2117 **BRAUNSTEIN, GLENN D.; & KOHLER, PETER Q.** Pituitary function in Hand-Schuller-Christian disease. Evidence for deficient growth hormone release in patients with short stature. *New England Journal of Medicine*, 286(23):1225-1229, 1972.

Thirteen Hand-Schuller-Christian disease (HSCD) patients (6 females) had 2 or more manifestations of the disease including osteolytic bone defects, diabetes insipidus (DI), exopthalmos, granulomatous otitis media, pulmonary interstitial infiltration or fibrosis, or dermatologic involvement. Eight were at or below the third percentile for stature, and 3 with normal stature were postpubertal. Growth hormone response (GH) to arginine, insulin, or pseudomonas polysaccharide pyrogen was below normal in 7 of 8 short-stature patients. Of the 5 with normal height, the 2 prepubertal patients had adequate GH response, and the 3 postpubertal, who had adult onset of HSCD, had abnormal GH response. Of the 7 short-statured, GH-deficient patients, 5 had glucose intolerance, and 4 had increased insulin sensitivity (as did 1 adult with inadequate GH). Urinary gonadotropin levels, gonadal function, plasma cortisol, & thyroid function were normal. Eight had complete DI, 2 had partial DI, and one was normal. Short stature, inadequate GH, and DI were coexistent in 6 of 8 short-statured patients. HSCD may result in a progressive loss of GH release and other findings such as delayed puberty, abnormal glucose tolerance, insulin sensitivity, and low ratio of height to bone age are consistent with inadequate GH. Other causes of growth failure including uncontrolled DI, prolonged glucocorticoid therapy, or malnutrition have been ruled out. The GH failure may be secondary to involvement of the hypothalamus. (55 refs.) - *V. J. Goldberg.*

National Institutes of Health
Bethesda, Maryland 20014

2118 **ROY, S.; SINGH, NAUNIHAL; DEO, M. G.; & RAMALINGASWAMI, V.** Ultrastructure of skeletal muscle and peripheral nerve in experimental protein deficiency and its correlation with nerve conduction studies. *Journal of the Neurological Sciences*, 17(4):399-409, 1972.

Ultrastructural alterations in skeletal muscle and peripheral nerve in protein deficient monkeys were correlated with nerve conduction studies in these animals. The Ss were 11 young male rhesus monkeys of which 8 animals received a protein deficient diet but with an adequate calorie supply and the 3 others served as controls. The protein-deficient animals showed a gradual loss of weight, wasting, and reduction of serum proteins. Atrophy of the muscle fibres with increase in sarcolemmal nuclei was striking in the protein-deficient animals. Ultrastructural studies showed

thinning of myofibrils associated with loss of myofilaments and the disappearance of Z-bands of one or more myofibrils. There was also a reduction of mitochondria and of sarcotubular elements. Peripheral nerves showed changes involving the myelin sheath in the form of infolding and formation of myelin nodules protruding into the axoplasm. The ultrastructural changes correlated well with nerve conduction studies. Serial studies showed marked slowing of conduction velocities at 9 weeks after deprivation of proteins. (28 refs.) - *A. C. Schenker.*

All India Institute of Medical Sciences
New Delhi-16, India

2119 **KALYANARAMAN, K.; CHAMUKUTTAN, SNEHALATA; ARJUNDAS, G.; GAJANAN, N.; & RAMAMURTHI, B.** Maple syrup urine disease (branched-chain ketoaciduria): variant type manifesting as hyperkinetic behaviour and mental retardation: report of two cases. *Journal of the Neurological Sciences*, 15(2):209-217, 1972.

Two siblings in a South Indian family with a nonfatal variant of maple syrup urine disease are described. The diagnosis of this disease was confirmed by the abnormally high levels of branched-chain amino acids, valine, leucine, and isoleucine in the serum and the markedly raised levels of keto acids in serum corresponding to those amino acids, together with their increased urine secretion. The children had MR with hyperkinetic behavior and skin and hair changes. These changes in hair and skin, although not a characteristic feature of maple syrup urine disease, may have been due to competitive inhibition between the branched-chain amino acids and essential nutritional factors responsible for the integrity of skin and hair. The inheritance was compatible with an autosomal recessive mode. A diet low in valine, leucine and isoleucine was effective in reducing the skin lesions on the face and in the reduction of keto acid in sera and urine. (18 refs.) - *A. C. Schenker.*

Madras Medical College
Madras-3, India

2120 **IONASESCU, VICTOR; STEGINK, LEWIS; MUELLER, SHIRLEY; & WEINSTEIN, MARY.** Amino acid abnormality in Sjogren-Larsson syndrome. *Archives of Neurology*, 28(3):197-199, 1973.

A case of Sjogren-Larsson syndrome is reported in which urinary excretion of glutamine, serine, glycine, and histidine was increased, while excretion of the other amino acids, including arginine, was normal. Most striking were the elevated glutamine levels in plasma, spinal fluid, urine, and erythrocytes. The patient was a 14-year-old boy with congenital ichthyosis, but with normal intelligence (IQ of 96-104); other abnormalities were: autosomal recessive inheritance, congenital ichthyosis, spastic paraparesis, macular degeneration, speech defects, hypertelorism, tooth anomalies and dermatoglyphic anomalies. The mechanism and significance of the increased glutamine contents are not known. (13 refs.) - *A. C. Schenker.*

University Hospitals
Iowa City, Iowa 52240

2121 **OLDENDORF, WILLIAM H.** Saturation of blood brain barrier transport of amino acids in phenylketonuria. *Archives of Neurology*, 28(1):45-48, 1973.

The effects of high serum phenylalanine in phenylketonuria (PKU) on the blood brain barrier (BBB) penetration of other amino acids were studied. Pooled PKU and control sera were used as the fluid vehicles for the injection into the rat carotid arterial system of 13 L-amino acids labeled with ^{14}C. The other fluid vehicles used were Ringer's solution at pH 7.55 and controls serum in which the phenylalanine concentration had been raised by addition of unlabeled phenylalanine. All of the amino acids exhibited the greatest uptakes when a Ringer's vehicle was used. The reduced uptake seen with the control serum was further reduced for most of the amino acids when the PKU serum vehicle was used, except for lysine, arginine, and ornithine. The control serum with added phenylalanine showed a saturation of amino acid uptakes resembling that seen with PKU serum. The use of dialyzed PKU serum resulted in an increased uptake of ^{14}C phenylalanine. The clinical implication of these studies is that saturation of BBB transport of several amino acids may be,

in some part, responsible for the MR in PKU. (14 refs.) - *A. C. Schenker.*

Wadsworth Hospital Center
Los Angeles, California 90073

2122 **MARTIN, J.-J.; & SCHLOTE, W.** Central nervous system lesions in disorders of amino-acid metabolism: a neuropathological study. *Journal of the Neurological Sciences,* 15(1):49-76, 1972.

Neuropathological data concerning various amino-acidurias (AA), and the main general features of the central nervous system lesions in this connection, are reviewed. The AAs are reviewed and tabulated under the subheadings of primary and secondary AAs, the former including data for: overflow AAs, such as hyperglycinemia, hyperprolinemia and hydroxyprolinemia, homocystinuria, Oasthouse urine disease, hyperpipecolatemia, tyrosinemia, maple syrup urine disease, diseases of the urea cycle, hyperammonemia associated with ornithine transcarbamylase deficiency, argininosuccinic aciduria (the classical and neonatal forms), which are all threshold AAs; the no-threshold AAs of which cystathioninuria is discussed; and the renal (transport) AAs, which include cystinuria and Hartnup's disease. Of the secondary AAs, only Lowe's syndrome is described. The main features of the central nervous system lesions are described under the glial changes, which include myelination and physiological fibrillary gliosis; the status spongiosus; myelin alterations; neuronal migration and maturation and neuronal alterations; and differential neuropathological diagnosis. (100 refs.) - *A. C. Schenker.*

University of Tubingen
Tubingen, German Federal Republic

2123 **DAVIES, D. P.** Plasma amino-acids of infants. *British Medical Journal,* 1(5798):512, 1972. (Letter)

Omission of the sampling time from a report on measurement of plasma amino-acid levels in low-birth-weight infants being given a high protein diet is significant. Recent observations establishing the existence of a circadian periodicity for total and individual plasma amino-acids in newborns make any quantitative studies of plasma amino-acids incomplete. (1 ref.) - *B. J. Grylack.*

Welsh National School of Medicine
Cardiff Royal Infirmary
Cardiff, Wales

2124 **RANDT, CLARK T.; & DERBY, BENNETT M.** Behavioral and brain correlations in early life nutritional deprivation. *Archives of Neurology,* 28(3):167-172, 1973.

Behavioral and brain changes, resulting from maximal early life undernutrition, were studied in DBA/2J mice. Behavioral tests evaluated: activity, open field test, feeding behavior, motivation, active avoidance learning, spatial discrimination learning reversals, and problem solving tests. The nutritionally deprived animals remained persistently stunted in their growth, despite the feeding of a normal diet from weaning at 21 days of age. Mean brain weight at birth was 20% lower for the offspring of undernourished dams. At 600 days, a 12% reduction in mean brain weight persisted. Histological examination of the brain revealed no differences between control and experimental groups. In the behavioral tests, exploratory behavior was significantly increased ($P<.01$) in the early life undernourished mice; these animals also consumed a larger number of meals than the controls ($P<.001$) and made more errors in problem solving ($P<.02$). The results may relate to an alteration in attention mediated by the more rostral portions of the reticular system. (39 refs.) - *A. C. Schenker.*

New York University Medical Center
New York, New York 10016

2125 **TAORI, G. M.; IYER, G. V.; MOKASHI, SHALINI; BALASUBRAMANIAN, K. A.; CHERIAN, R.; CHANDI, SUSHIL; JOB, C. K.; & BACHHAWAT, B. K.** Sanfilippo syndrome (mucopolysaccharidosis-III). *Journal of the Neurological Sciences,* 17(3):323-345, 1972.

Two cases of mucopolysaccharidosis (MPS) type III, the Sanfilippo syndrome, are described, giving details of clinical, radiological, histopathological, and biochemical features, and compared with cases in the literature. In both cases facial features were very coarse; in one case overt corneal clouding was present. One of the cases, an 11-year-old boy, behaved in a destructive and hyperkinetic manner, whereas the other, a 7-

year-old boy, though MR, was docile. Beaking and kyphosis of the vertebral bodies were seen in one case, whereas they were mild in the other; both showed biconvex vertebrae on skiagrams of the spine. Group muscle fibre atrophy and EMG findings of fibrillation suggest the involvement of lower motor neurons. Changes in cortical neurons which were ballooned with PAS-positive lipid material were seen in both cases. The intraneuronal zebra-bodies, seen under electron microscopy, are thought to be due to accumulation of ganglioside, resembling those seen in Tay-Sachs disease. In the brain tissue of both cases, heparan sulfate was markedly increased differentially, and dermatan sulfate was somewhat increased in one case. Glycosaminoglycans were markedly increased in the one case in which this analysis was done. (39 refs.) - *A. C. Schenker.*

Christian Medical College Hospital
Vellore-7, South India

2126 **PERCY, ALAN K.; McCORMICK, URSULA M.; KABACK, MICHAEL M.; & HERNDON, ROBERT M.** Ultrastructure manifestations of G_{M1} and G_{M2} gangliosidosis in fetal tissues. *Archives of Neurology, 28(6):417-419, 1973.*

Four cases are reported, 3 of Tay-Sachs disease (G_{M2} gangliosidosis) and 1 of G_{M1} gangliosidosis, in which membranous cytoplasmic bodies were seen in the neurons of the midterm fetus, indicating that structural manifestations were already present at an early stage of gestation. In the cord samples from the 4 abnormal fetuses, nuclear margination was prominent in the anterior horn cells. Numerous globular structures, seen in the cytoplasm, were felt to represent developing membranous cytoplasmic bodies. On electron microscopic examination, these neurons were seen to contain numerous whorls of laminated lipid material. The structures are less compact than typical mature membranous cytoplasmic bodies. (11 refs.) - *A. C. Schenker.*

Charles R. Drew Postgraduate Medical School
Los Angeles, California 90059

2127 **DEKABAN, ANATOLE S.; & CONSTANTOPOULOS, GEORGE.** Mucopolysaccharidoses: Relation of elevated cerebral spinal fluid to mental retardation. *Archives of Neurology,* 28(6):385-388, 1973.

A study in 14 patients with 4 major types of mucopolysaccharidosis is reported in which levels of acid mucopolysaccharide (AMPS) in the cerebrospinal fluid (CSF) were found to correlate with the degree of mental impairment. Of the 14 patients, 3 had type I (Hurler), 2 had type II (Hunter), 6 had type III (Sanfilippo), and 3 had type V (Scheie) mucopolysaccharidosis. All patients excreted excessive amounts of AMPS in their urine. Eleven patients showed elevations of AMPS in the CSF ranging from 7-fold to over 25-fold above normal control values; 2 patients had normal levels; and 1 patient had only a 3-fold increase of AMPS in the CSF. The last 3 patients had an unimpaired intellect. The finding that a number of patients with this anomaly have normal serum levels of AMPS and greatly elevated levels in the CSF suggests that AMPS may have derived from the central nervous system. The principal AMPS involved are the partially degraded dermatan sulfate (DS) and heparin sulfate (HS). Patients with types I, II, and III showed that 54-100% of the total AMPS in their CSF was HS; these were the patients with the most marked mental deterioration. (25 refs.) - *A. C. Schenker.*

National Institutes of Health
Bldg. 10, Room 4N-248
Bethesda, Maryland 20014

2128 **GRUNNET, MARGARET L.; & SPILSBURY, PAUL R.** The central nervous system in Fabry's disease: an ultrastructural study. *Archives of Neurology,* 28(4):231-234, 1973.

Intraneuronal inclusions in the brain seen in a case of Fabry's disease are described which are unlike those reported in skin, kidney, or blood vessels. Throughout the CNS, intracytoplasmic inclusions were seen about small blood vessels in perithelial and endothelial cells; the unique inclusion consisted of concentric whorling of dark and light bands around an amorphous or granular core. These bodies superficially resembled the membranous cytoplasmic bodies seen in Tay-Sachs disease, and also resembled zebra bodies on end. Some cases without evidence of intraneural inclusions may indicate several incom-

plete forms of Fabry's disease or genetic variants. (6 refs.) - *A. C. Schenker.*

University of Utah College of Medicine
Salt Lake City, Utah 84112

2129 **BARCLAY, G. P. T.; & PATH, M. R. C.** Pseudocholinesterase activity as a guide to prognosis in malnutrition. *American Journal of Clinical Pathology*, 59(5):712-716, 1973.

Pseudocholinesterase activity was assayed in 302 children with kwashiorkor, marasmus, or a mixed syndrome, with a view to using such assay for diagnosis and prognosis. Samples of blood were tested and cores of liver were obtained for histologic examination from 43 children. Fatty infiltration was demonstrated in the livers of 30 of the 35 children with severe kwashiorkor and in 2 of 8 marasmic children. Of the children with known malnutrition, 83% has pseudocholinesterase levels below the lower limit of normal (55 units/ml). All patients whose enzyme responses (by serial assay) were greater than 10 units/ml/week, following admission, survived; however, 8 of the survivors had less than 5 units/ml/week, with 5 children showing satisfactory responses on further assays. Serial pseudocholinesterase assays offer a sensitive early index of hepatic dysfunction in severe forms of malnutrition. (14 refs.) - *A. C. Schenker.*

Box 8285 Causeways
Salisbury, Rhodesia

2130 **TEN KATE, L. P.; & ANDERS, G. J. P.** A. Serum dependency of cellular phenotype in mucopolysaccharidoses: the influence of autologous serum on metachromasia. *Humangenetik*, 18:95-98, 1973.

Experiments with fibroblasts from a patient with Hurler's disease and from a patient with Sanfilippo's disease confirmed a previous report that metachromasia of cells from patients with mucopolysaccharidosis disappears if fetal calf serum is replaced by normal human serum in the culture medium. The fibroblast cultures were obtained from skin biopsies of the 2 patients; these cultures, grown in a medium supplemented with fetal calf serum, were positive for metachromasia and polarization after staining with toluidine blue 0. This effect was not obtained when the fibroblasts were grown either in a medium of normal human serum or in serum taken from the patient. The correction of cellular metachromasia by normal human serum does not depend on the presence of a corrective factor absent in the sera of these patients. (10 refs.) - *A. C. Schenker.*

State University Groningen
Groningen, The Netherlands

2131 **BRADFORD, WILLIAM D.; WILSON, JAMES W.; & GAEDE, JANE T.** Primary neonatal hyperparathyroidism—an unusual cause of failure to thrive. *American Journal of Clinical Pathology*, 59(2):267-275, 1973.

An infant with failure to thrive and a complicated clinical course on postmortem examination revealed findings of hyperparathyroidism. The patient was a 6-day-old female infant, admitted to hospital because of lethargy and poor feeding. On clinical examination the child was mildly jaundiced and markedly hypotonic; the total protein was 4.5gm/100ml and the total bilirubin was 8.6mg/100ml (direct 0.5). Radiologic examination showed a coarseness of trabecular pattern, a decrease in density, and pronounced subperiosteal resorption in the small bones of the hands, ribs, and of the legs and the pelvic bones. At 33 days of age the infant developed respiratory distress and generalized edema and died. The diagnosis of neonatal hyperparathyroidism was established by the characteristic radiologic picture of osteitis fibrosa cystica, enlargement of the parathyroid glands, and the presence of calcification in soft tissues and organs. Successful treatment of this condition in infants requires prompt diagnosis and surgical removal of all or part of the parathyroid gland. (18 refs.) - *A. C. Schenker.*

Duke University Medical Center
Durham, North Carolina 27710

2132 **MILUNSKY, AUBREY; & NEUFELD, ELIZABETH F.** The Hunter syndrome in a 46 XX girl. *New England Journal of Medicine*, 288(2):100-101, 1973.

A case of clinically expressed and biochemically characterized Hunter syndrome is reported in a girl of normal karyotype. This 22-month-old patient had severe psychomotor retardation, moderate bilateral spasticity, and hepatosplenomegaly. She had coarse facies and appeared deaf. Her younger brother, age 11 months, was also severely affected. The mother had Gaucher's disease, and the father and the first child were in good health. Marked mucopolysaccharidiuria was observed in both. Fibroblasts cultured from skin biopsies of the 2 affected children were deficient in Hunter factor. Because of her karyotype and her normal father, the affected girl must be considered a heterozygote for the syndrome. The most likely explanation for her clinical manifestations is thought to be the selection *in vivo* of the cells in which the maternal X-chromosome is expressed. (7 refs.) - *A. C. Schenker.*

Massachusetts General Hospital
Boston, Massachusetts

2133 **BOOTH, CAROL W.; & NADLER, HENRY L.** In vitro selection for the Hunter gene. *New England Journal of Medicine*, 288(12):636, 1973. (Letter)

Reference is made to the reported occurrence of Hunter's syndrome in a 46,XX girl. This observation could be interpreted as indicating a selected advantage for the cells whose active X-chromosome carrier is the gene for Hunter's syndrome. A similar phenomenon has been observed in cultures of skin fibroblasts derived from Hunter heterozygotes. Mucopolysaccharide metabolism can be followed in such cultures by observation of the cellular accumulation of labels when radioactive sulfate is added to the tissue culture medium. Distinctly abnormal accumulation of radioactive sulfate has been noted in cultures from 3 Hunter heterozygotes, which are reported. The findings suggest that cells mutant for the Hunter gene have a selective advantage over normal cells in tissue culture. (3 refs.) - *A. C. Schenker.*

Children's Memorial Hospital
Chicago, Illinois

2134 **LOWDEN, J. ALEXANDER; CUTZ, ERNEST; CONEN, PATRICK E.; RUDD, NOREEN; & DORAN, TERRANCE A.** Prenatal diagnosis of G_{M1}-gangliosidosis. *New England Journal of Medicine*, 288(5):225-228, 1973.

A case in which the prenatal diagnosis of G_{M1}-gangliosidosis was confirmed by biochemical and morphologic studies in the fetus is presented. The parents were cousins with a common paternal grandfather and paternal grandmothers who were sisters, and had had 1 previous child with G_{M1}-gangliosidosis who died at 13 months of age. Amniocentesis was performed on the mother when she became pregnant 2 years later, at 14 weeks' gestation. Betagalactosidase activity was absent in the amniotic fluid; enzyme analyses of the cultured amniotic fluid cells confirmed the diagnosis of an affected fetus. The pregnancy was terminated at 17 weeks of gestation. In the fetus, vacuolation and abnormal inclusions were seen by light and electron microscopy in epon-embedded sections from brain, liver, kidney, and other organs. Electron micrographs of dorsal root ganglion neurons showed typical zebra bodies. Storage was identified in 1-micron sections of the tissue and was far more advanced in the placenta. The importance of morphologic findings to confirm the biochemical data is stressed. (34 refs.) - *A. C. Schenker.*

Research Institute Hospital for Sick Children
Toronto 2, Canada

2135 **BRADLEY, W G.; JENKISON, MARGARET; PARK, DOROTHY C.; HUDGSON, P.; GARDNER-MEDWIN, D.; PENNINGTON, R. J. T.; & WALTON, J. N.** A myopathy associated with lipid storage. *Journal of the Neurological Sciences*, 16(2):137-154, 1972.

Spontaneous remission in a 23-year-old woman of proximal myopathy associated with high levels of sarcoplasmic lipid is reported. The patient had suffered 2 attacks of the muscle weakness; the first, 15 months prior to the main illness, which remitted after a few weeks; and the second, also beginning to remit 18 months after its onset, which improved to a state of clinical normalcy after a further year. The most striking feature of this case was the marked increase in neutral lipid in the muscle fibers during the height of the illness. The high lipid content of the muscle was not associated with the presence of any unusual fatty acid. Since there is normally a rapid turnover of muscle lipids, the increased amounts in this patient might be due either to increased synthesis or to decreased mobilization of lipid. Morphological abnormalities and excessive numbers of skeletal muscle mitochondria were seen in the second deltoid muscle biopsy. (24 refs.) - *A. C. Schenker.*

Newcastle General Hospital
Newcastle upon Tyne, England

2136 **CZLONKOWSKA, ANNA.** A study of haemolysis in Wilson's disease. *Journal of the Neurological Sciences*, 16(3):303-314, 1972.

The cause of hemolysis in some cases of Wilson's disease was investigated in 30 patients (22 males, 8 females) with clinical symptoms of Wilson's disease as compared with a control population. The serological investigations included: globulins absorbed by red cells; warm incomplete autoantibodies; cold autoantibodies; and hemolysis. Biochemical determinations included: reduced glutathione (GSH), activity of glucose-6-phosphate dehydrogenase (G-6-PD) (E.C.1.1.1.49) and 6-phosphogluconate dehydrogenase (6-PGD) (E.C.1.1.1.43), and hexokinase activity (E.C.2.7.1.1.) in red cells. No patient presented symptoms of hemolysis. Despite the increased level of cold antibodies, it seems that cold agglutinins are not the cause of hemolysis; such increased levels in the patients are probably due to immunological dysfunction caused by liver cirrhosis. The fact that hemolysis was observed in sera without complement excludes the immunological character of the hemolysis. It is suggested that, during hemolytic crises, the increased copper level in serum, causing a drop in GSH, may be one of the causes of hemolysis. The activities of G-6-PD and 6-PGD were normal. (43 refs.) - *A. C. Schenker.*

Psychoneurological Institute
Pruszkow k Warszawy, Poland

2137 **WADLINGTON, W. B.; & *RILEY, HARRIS D.** Familial disease characterized by neonatal jaundice, and probable hepatosteatosis and kernicterus: a new syndrome? *Pediatrics*, 51(2):192-198, 1973.

The findings in a family composed of 11 children, of which 5 of the males died within 2 weeks after birth with jaundice, abdominal enlargement, and neurologic abnormalities, are reported. The most striking findings at necropsy were extensive hepatosteatosis and kernicterus. Autopsy in one of the cases revealed an enlarged liver which was heavily infiltrated with fat; microscopic examination revealed that virtually the entire parenchyma was replaced by fat. The most striking finding in the brain was the intense golden yellow stain of almost all the nucleated areas in the midbrain and cerebellum. There was a marked increase in the concentration of total lipids and fatty acids in the liver. It is suggested that an inborn error of metabolism was responsible for this seemingly familial disease. (23 refs.) - *A. C. Schenker.*

Children's Memorial Hospital
University of Oklahoma Health Sciences Center
Oklahoma City, Oklahoma 73190

2138 **EL SHAHAWY, M.** Effective renin activity in plasma of children with kwashiorkor. *Lancet*, 1(7762):1241, 1972. (Letter)

Magnesium deficiency, which has been shown in previous studies to play an important role in the protein-calorie malnutrition syndrome, should be considered as a possible etiological factor for the increased renin activity characteristic of kwashiorkor cases. If this theory is valid, addition of magnesium salts to the regimen in kwashiorkor syndrome cases could benefit the patient by correcting high plasma-renin levels. (6 refs.) - *N. Mize.*

Medical College of Georgia
Augusta, Georgia 30902

2139 **COOK, ROBERT.** Treatment of malnourished children. *Lancet*, 1(7750):593-594, 1972. (Letter)

General agreement as to the ineffectiveness of most hospital treatment of severe malnutrition in children does not mean, however, that the building of pediatric hospitals in developing countries should be discouraged. Rather, the gross disparity between the high childhood mortality rate and the number of available pediatric beds supports the editorial suggestion that routine cases of severe malnutrition be treated at under-5 clinics or at nutrition rehabilitation centers—thereby freeing badly needed hospital space for the treatment of other pediatric conditions. Additionally, while cheap food supplements are necessary now, no fundamental solution to the malnutrition problem will be brought about until the general standard of living in developing countries is measurably improved. (2 refs.) - *N. Mize.*

Caribbean Food and Nutrition Institute
PO Box 140, Kingston 7, Jamaica

2140 **KRITZINGER, E. E.; BLAKE, G. T. W.; KANENGONI, E.; & JONES, J. J.** Effective renin activity in plasma of children with kwashiorkor. *Lancet*, 1(7764):1333-1334, 1972. (Letter)

The results of a recent Rhodesian study fail to support previous suggestions that magnesium deficiency might account for the high plasma-renin activity in kwashiorkor patients. In two groups of patients, no correlation ($p > 0.1$) was found between plasma-renin activity and serum-magnesium rates. Children participating in the survey who received a standard electrolyte supplement generally experienced a significantly greater fall in renin activity. Additionally, of the 12 factors considered to be possibly related to the prognosis of kwashiorkor patients, multiple regression analysis showed that renin accounted for 14.4% of the total variation while magnesium accounted for only 0.61%. - *N. Mize.*

University of Rhodesia
Salisbury, Rhodesia

2141 **WILLIAMS, CICELY D.** Protein-calorie malnutrition. *Lancet*, 1(7764):1333, 1972. (Letter)

The tendency to automatically label all obvious cases of malnutrition as "protein-calorie malnutrition" (PCM), before the actual protein status or calorie intake has been determined, cannot help but contribute to more unfortunate instances of misdiagnosis and inadequate treatment. It is extremely important that physicians take the time to adequately distinguish among cases of acute and chronic PCM, beriberi, worms, and malabsorption and other diseases such as tuberculosis, hepatitis, or diarrhea. These conditions share many of the same symptoms—weight loss, edema, anorexia—but require different treatments. PCM can be accurately identified by measurement of the serum-protein or serum-albumin levels. - *N. Mize.*

Tulane University School of Public Health
and Tropical Medicine
New Orleans, La. 70112

2142 **PUNNETT, HOPE H.** Hunter syndrome in girl (cont.). *New England Journal of Medicine*, 288(16):856, 1973. (Letter)

An alternative explanation to that offered by Milunsky and Neufeld, with respect to a case of Hunter syndrome in a 46XX girl, is that she is homozygous, having inherited one mutant Hunter gene from her presumed carrier mother and a second newly mutated gene from her father. It is only in exceptional circumstances, such as this, that the origin of a spontaneous recessive mutation is detectable. Experimentally in drosophila or mice, irradiated males are mated to genetically marked females to detect new mutations. The X chromosome is no less vulnerable to mutation than the autosomes. An analogous situation presented evidence for a new mutation at the transferase locus that produced the galactosemic heterozygous state in the mother of a child with galactosemia when neither of the maternal grandparents was a heterozygote for this defect. - *A. C. Schenker.*

St. Christopher's Hospital for Children
Philadelphia, Pennsylvania

2143 **DONTANVILLE, VIRGINIA K.; & *CUNNINGHAM, GEORGE C.** Effect of feeding on screening for PKU in infants. *Pediatrics*, 51(3):531-538, 1973.

The effect of the amount of phenylalanine ingested on the screening levels of phenylketonuric (PKU) infants was studied to discover whether such cases might be missed if feeding was not rigorously controlled. The study population comprised 108 infants with PKU; all had been screened and all but 2 were tested by 9 days of age. Eleven had negative screening tests but were detected later through blood and urine testing. Approximately half the infants had the screening test taken on the second day of life; 20% were tested by 48 hr of age; 50% by 62 hr; and 75% by 72 hr. The range of phenylalanine intake was from 0 to over 3,000mg. All but one of the 27 infants who had ingested less than 200mg of phenylalanine exceeded the 4mg screening level. Of the 11 infants whose screening test was negative, only one had ingested less than 200mg of phenylalanine. Although there was a gradual increase in the mean phenylalanine levels of the PKUs as the intake of phenylalanine increased, no relationship was established between the phenylalanine content of the feedings and the test results. (9 refs.) - *A. C. Schenker.*

Bureau of Maternal and Child Health
Department of Public Health
Berkeley, California 94704

2144 **SUSKIND, ROBERT M.; *OLSON, LLOYD C.; & OLSON, ROBERT E.** Protein calorie malnutrition and infection with hepatitis-associated antigen. *Pediatrics*, 51(3):525-530, 1973.

The effect of undernutrition on host susceptibility to infection with hepatitis-associated antigen (HAA) was studied in northern Thai children ranging in age from 1 to 5 years. Fourteen of 48 patients who were admitted with severe protein calorie malnutrition (PCM) were positive for HAA at some time during hospitalization; 6 Ss were positive at the time of admissions and 4 remained positive throughout hospitalization; 8 patients were negative for HAA on admission and subsequently became positive. Although the mechanism mediating the apparent increased susceptibility to HAA infection is unknown, it is of interest that PCM has been shown to be associated with defects in cellular immunity. The results suggest the possibility that the increased incidence of HAA infection (29% as compared to 6.4% of normal children in the same area) in Thailand, as well as in other areas of the developing countries, may be secondary to both increased exposure and to depression of host defense mechanisms as a result of less severe nutritional deficiencies. (17 refs.) - *A. C. Schenker.*

The Rockefeller Foundation
Bangkok, Thailand

2145 **WEINBERG, ARTHUR G.; MCCRACKEN, GEORGE H.; LOSPALLUTO, JOSEPH; & LUBY, JAMES P.** Monoclonal macroglobulinemia and cytomegalic inclusion disease. *Pediatrics*, 51(3):518-524, 1973.

A case of chronic cytomegalovirus infection and monoclonal kappa-type macroglobulinemia is presented in an 8-month-old infant. The latter was first observed at 4 months of age and persisted until death at 8 months. IgM values of 2,500-3,200mg/100ml were observed in all sera, except for a specimen at 8 months when the IgM was 960mg/100ml. Fluorescent and neutralizing antibody against cytomegalovirus was demonstrated in the patient's IgG fraction of serum. IgG-, IgM-, and IgA-producing plasma cells were identified in the spleen, thymus, and lymph nodes at autopsy. It is possible that a primary cytomegalovirus infection induced the development of the immunoglobin abnormality. This monoclonal macroglobulinemia appears to be the first case recorded in infants with cytomegalovirus infection. (19 refs.) - *A. C. Schenker.*

Children's Medical Center
1935 Amelia St.
Dallas, Texas 75235

2146 **PINCUS, JONATHAN H.; COOPER, JACK R.; MURPHY, JEROME V.; RABE, EDWARD F.; LONSDALE, DERRICK; & DUNN, HENRY G.** Thiamine derivatives in subacute necrotizing encephalomyelopathy: a preliminary report. *Pediatrics*, 51(4):716-721, 1973.

Treatment with thiamine propyl disulfide (TPD) and thiamine tetrafuryldisulfide (TTFD) in cases of children with subacute necrotizing encephalomyelopathy (SNE) is described as being more effective in raising body fluid levels of the vitamin than regular thiamine. This conclusion is

based on a study in 21 children in whom the effect of oral therapy with large doses of thiamine (0.6-4.0gm/day), TPD (0.15-0.8gm/day) and/or TTFD (0.5-1.0gm/day), were followed. The Ss were divided into 2 groups: Group 1 (12 Ss) comprised children with an assured diagnosis of SNE; and Group 2 (9 Ss) comprised more benign forms. Though data are preliminary, a comparison of the efficacy of regular thiamine and its derivatives in raising thiamine levels in various body fluids revealed that the substituted compounds resulted in higher blood and CSF levels. The transport across membranes of both TPD and TTFD, unlike thiamine hydrochloride, is not limited with respect to dosage, the i.v. route being more effective in raising the CSF thiamine concentration, which seems to correlate with remissions. (16 refs.) - *A. C. Schenker.*

Yale University School of Medicine
New Haven, Connecticut 06510

2147 **MURPHY, JEROME V.** Subacute necrotizing encephalomyelopathy (Leigh's disease): detection of the heterozygous carrier state. *Pediatrics*, 51(4):710-715, 1973.

The results of an analysis of urine specimens collected from families of 4 patients with subacute necrotizing encephalomyelopathy (SNE) for inhibition to phosphotransferase were compared to those from a control population, to discover if this SNE inhibitor is present in carriers of SNE. Urines from the control population inhibited the phosphotransferase 0-10%; the 7 parents of the 4 patients inhibited the enzyme 25.4-38.6%; and the percent inhibition by urines of other relatives varied between 0 and 26%. Two untreated patients with SNE had 34.6% and 37.4% inhibition by this method. The studies demonstrated that obligate heterozygous carriers for SNE have significant amounts of the inhibitor thiamine pyrophosphate (TTP) synthesis in their urine. Since the inhibitor is variably present in the blood of parents and is consistently present in blood from SNE patients, it may be the amount of inhibitor in blood and spinal fluid which produces the clinical picture of Leigh's disease. Detection of heterozygous carriers is possible by the urine assay for phosphotransferase inhibition. (15 refs.) - *A. C. Schenker.*

Children's Hospital of Pittsburgh
Pittsburgh, Pennsylvania 15213

2148 **PORTER, BASIL A.; REFETOFF, SAMUEL; *ROSENFIELD, ROBERT L.; DE GROOT, LESLIE L.; FANG, VICTOR S.; & STARK, V.** Abnormal thyroxine metabolism in hyposomatotrophic dwarfism and inhibition of responsiveness to TRH during GH therapy. *Pediatrics*, 51(4):668-674, 1973.

The effects of human growth hormone (GH) administration on GH deficient dwarfs were studied in 5 hyposomatotrophic dwarfs and one normal child, to test the hypothesis that hypothyroidism resulted from suppression of thyrotropin (TSH) release by GH. Synthetic thyrotropin-releasing hormone (TRH) stimulation tests were performed before and after short-term administration of GH. The TSH, which was normal prior to GH administration in all Ss, was blunted in response to TRH following GH administration. The degree of blunting was variable and independent of thyroid function status. GH may directly inhibit the response of the thyroxine. GH therapy may have corrected a state of functional hypothyroidism, resulting in diminished TSH response to TRH. The studies indicate that a state of relative hypothyroidism exists which is undetectable by measurement of serum total and free thyroxine. (19 refs.) - *A. C. Schenker.*

University of Chicago Hospitals
Chicago, Illinois 60637

2149 **DANKS, DAVID M.; CAMPBELL, PETER E.; STEVENS, BRIAN J.; MAYNE, VALERIE; & CARTWRIGHT, ELIZABETH.** Menkes's kinky hair syndrome: an inherited defect in copper absorption with widespread effects. *Pediatrics*, 50(2):188-201, 1972.

Study of 7 cases of Menkes' kinky hair syndrome among 5 families has indicated that the basic biochemical defect in this syndrome involves the intestinal absorption of copper and that all of the features of the disease are the direct or indirect result of copper deficiency. MR, hypothermia, convulsions, and growth retardation were common clinical features, and all patients showed a striking facial resemblance to one another marked by pallor and lack of expressive movement and by pudgy cheeks and horizontal and twisted eyebrows. Characteristic hair changes, radiologic features, and a seborrheic rash provided helpful clues for diagnosis. Arterial

tortuosity was demonstrated throughout the body, and microscopic investigation revealed fragmentation and disintegration of the internal elastic lamina of arteries together with an irregular thickening of the intima. Four of the 5 families provided further support for an X-linked mode of inheritance for this condition. The frequency of the disease was estimated to be approximately 1 in 35,000 live births. Copper intravenously administered into ceruloplasmin is absorbed normally. Since treatment by parenteral copper seems a possibility, early diagnosis is especially important. (20 refs.) - *B. J. Grylack.*

Royal Children's Hospital Research Foundation
Parkville 3052, Victoria, Australia

2150 **CHASE, H. PETER; WELCH, N. NOREEN; DABIERE, CAROL S.; VASAN, N. S.; & BUTTERFIELD, L. JOSEPH.** Alterations in human brain biochemistry following intrauterine growth retardation. *Pediatrics*, 50(3):403-411, 1972.

Analyses of brains from 6 small-for-gestational age (SGA) infants and 10 appropriate-for-gestational age (AGA) infants for alterations in cellularity, protein, and lipid content have shown reductions in brain weight and cellularity in the SGA infants to be more marked in the cerebellum than in the remainder of the brain. In SGA infants, weight and cellularity were reduced 37% and 35%, respectively, in the cerebellum as compared with reductions of only 21% and 19%, respectively, in all other areas of the brain. Cholesterol content was statistically lower ($p<.05$) in the brains of the 4 term SGA infants than the 7 control infants, and the cerebroside and sulfatide fractions from each brain, analyzed together, were statistically lower ($p<.01$) in total content or in concentration in the brains from these 4 SGA infants as compared with the others. Galactolipid sulfotransferase activity was also reduced significantly ($p<.01$) in the brains from the SGA infants. While the brain alterations found in the infants who died appear to be more striking than those in SGA infants who survive the perinatal period, it is probable that many surviving infants also have these alterations at birth. (31 refs.) - *B. J. Grylack.*

University of Colorado Medical Center
Denver, Colorado 80220

2151 **URRUSTI, J.; YOSHIDA, P.; VELASCO, L.; FRENK, S.; ROSADO, A.; SOSA, A.; MORALES, M.; YOSHIDA, T.; & METCOFF, J.** Human fetal growth retardation: I. Clinical features of sample with intrauterine growth retardation. *Pediatrics*, 50(4):547-558, 1972.

One hundred and twenty-eight mother-newborn infant pairs were assessed for intrauterine growth and for anthropometric and clinical aspects of intrauterine growth failure. The 36 small-for-gestational age infants, who manifested the typical signs of intrauterine growth retardation, had a head circumference that was smaller than that of normal term babies and comparable to that of premature infants appropriately sized for a gestational age 5 weeks less than their own. Head circumference in 28 (78%) of these 36 infants and body length in 25 (70%) of them was below the twenty-fifth percentile for normal term infants. Of the 12 neonatal deaths that occurred, 3 involved infants with intrauterine growth retardation and 9, premature infants. The former took place within the first 24 hours of life, while 7 of the deaths observed in the second group happened during the first 72 hours. Neither maternal age nor number of pregnancies was found to be related to the severe impairment of intrauterine growth observed. Toxemia was evidently involved in gestational anomalies in 1 of 4 low-birthweight infants and 1 of 12 full-term infants. (48 refs.) - *B. J. Grylack.*

University of Oklahoma
Oklahoma City, Oklahoma

2152 **YOSHIDA, T.; METCOFF, J.; MORALES, M.; ROSADO, A.; SOSA, A.; YOSHIDA, P.; URRUSTI, J.; FRENK, S.; & VELASCO, L.** Human fetal growth retardation: II. Energy metabolism in leukocytes. *Pediatrics*, 50(4):559-567, 1972.

A study was conducted to establish the existence of any unique pattern for certain cell energy functions in leukocytes of mothers and their small-for-gestational age (intrauterine malnutrition, IUM) infants at the time of birth and to determine similarities or differences between these patterns and those of infants with severe postnatal protein-calorie malnutrition. Leukocyte cell size, as reflected by the protein-DNA ratio, was increased only in the IUM mother-infant

groups (cord blood) as compared with the normal full-term and premature appropriately-sized-for-gestation age groups. The adenosine triphosphate (ATP) and total adenine nucleotide content and the pyruvic kinase (PK) and adenylate kinase (AK) activity were significantly lower in leukocytes of IUM infants than in those of the other 2 infant groups. The energy capacity of leukocytes of the IUM mother-infant pairs was significantly lower than that of the other 2 groups. On the basis of the concept of "energy capacity," leukocytes of the IUM infants appeared to have defects in cellular energy metabolism similar to that seen in leukocytes of infants with postnatal protein-calorie malnutrition, and leukocytes of the mothers had a similar defect of energy metabolism. (42 refs.) - *B. J. Grylack.*

University of Oklahoma
Oklahoma City, Oklahoma

2153 **ROSADO, A.; BERNAL, A.; SOSA, A.; MORALES, M.; URRUSTI, J.; YOSHIDA, P.; FRENK, S.; VELASCO, L.; YOSHIDA, T.; & METCOFF, J.** Human fetal growth retardation: III. Protein, DNA, RNA, adenine nucleotides and activities of the enzymes pyruvic and adenylate kinase in placenta. *Pediatrics*, 50(4):568-577, 1972.

An analysis was made of the placentas obtained at the moment of delivery from mother-infant pairs comprising 35 small-for-gestational age infants considered as having intrauterine malnutrition (IUM), 28 premature but appropriately-sized-for-gestational age infants (AGA), and 17 normal full-term (FT) infants. The ratio of placental weight:infant weight was significantly higher for IUM than FT infants, and the sizes of placentas of IUM infants were not markedly different from those of low-birthweight AGA infants, who also had a placental weight:infant weight ratio greater than that of FT infants. No correlation was shown between DNA content/g of placental tissue and fetal weight in any of the 3 groups. The highest RNA/DNA ratio (cytoplasmic mass per nuclear mass) was found in the IUM placentas. There was a good correlation between this ratio and adenylate kinase (AK) and pyruvic kinase (PK) activity in all groups studied. The low-birthweight AGA infant, born prematurely but in an active growth phase, showed a placental energy charge double that of the other groups, yet the "energy capacity" AK X (adenosine triphosphate + ½ adenosine diphosphate) was highest in IUM placentas and lowest in the premature AGA placentas. The lack of relevant differences in metabolic parameters between FT and IUM placentas suggests that either the metabolic imbalance is not reflected in placenta tissue, or that some other uninvestigated biochemical changes are connected more directly with intrauterine malfunction, or that the placenta does not reflect the prior growth process of the fetus or the metabolic maternal state. (21 refs.) - *B. J. Grylack.*

Hospital de Pediatria
Mexico, D.F.

2154 **ERICKSON, ROBERT P.; SANDMAN, ROBERT; ROBERTSON, WILLIAM VAN B.; & EPSTEIN, CHARLES J.** Inefficacy of fresh frozen plasma therapy of mucopolysaccharidosis II. *Pediatrics*, 50(5):693-701, 1972.

Clinical studies failed to demonstrate any effect of short-term treatment with large infusions of fresh frozen plasma on 5 male children with mucopolysaccharidosis II from 2 families. Single-blind evaluation showed no significant effect of 50ml/kg of fresh frozen plasma on clinical performance, on the quantity and size of urinary glycosaminoglycans, on the abnormal skin activity levels of β-galactosidase, β-glucuronidase, and N-acetylglucosaminidase, or on the size of leukocyte metachromatic granules. It was hoped that the abnormal levels of the acid hydrolases in the skin would revert towards normal if treatment were successful, but the point at which a second skin biopsy was performed, 2 to 3 days after the infusion, might have been too soon to detect such changes. It is possible that the propositi belonged to different subclasses of mucopolysaccharidosis II than a patient recently reported benefited by this therapy. (32 refs.) - *B. J. Grylack.*

University of California
San Francisco, California 94122

2155 **BRUNETTE, MICHELE G.; DELVIN, EDGARD; HAZEL, BERNARD; & SCRIVER, CHARLES R.** Thiamine-

responsive lactic acidosis in a patient with deficient low-Km pyruvate carboxylase activity in liver. *Pediatrics*, 50(5):702-711, 1972.

An account of an abnormality in pyruvate metabolism in a female infant with profound psychomotor retardation suffering from severe intermittent lactic acidosis illustrates the apparent pathogenesis of the hypoglycemia identified in the newborn period, the role of adrenocorticotropic hormone (ACTH) in provoking her lactic acidosis, hyperpyruvicacidemia, and hyperalaninemia, and the amelioration of lactic acidosis following pharmacologic doses of thiamine or selection of diet. The lactate-pyruvate ratio was normal at all times during episodes of lactic acidosis and alanine accumulation was proportional to that of pyruvate, thus implying a defect in pyruvate disposal. A deficiency of the low Michaelis constant component of pyruvate carboxylase activity in the liver was identified. The significant fall in the overall level of leucine, isoleucine, valine, threonine, phenylalanine, and tyrosine in plasma during high-carbohydrate feeding seemed to reveal the normal response to insulin, yet alanine remained elevated in plasma. When the diet provided adequate calories without imbalance of protein or carbohydrate, the accumulation of pyruvate and alanine could be restrained, and lactic acidosis was prevented. The high-affinity component of pyruvate carboxylase activity which is most effective at normal physiological concentrations of pyruvate was missing in the proposita; pyruvate carboxylation was relegated therefore to the other component, requiring a much higher concentration of pyruvate for conversion to oxaloacetate. (42 refs.) - *B. J. Grylack.*

Maisonneuve Hospital
Montreal 410, Quebec, Canada

2156 U.S. Health Services and Mental Health Administration, Maternal and Child Health Service. *Feeding the Handicapped Child.* Smith, Mary Ann Harvey, ed. Tennessee University, Child Development Center, Memphis, 1972, 157 p. $3.50. (Abstract)

Thirty-five brief papers discuss nutrition and the handicapped child. Topics include interdisciplinary approaches to nutrition services, recommended dietary allowances, inborn errors of metabolism, the role of undernutrition in MR, feeding skill training, childhood obesity, and the anatomy and physiology of oral musculature as related to speech. Case studies illustrate nutritional assessment procedures. - *B. J. Grylack.*

Child Development Center
Department of Nutrition
Memphis, Tennessee 38105s,

2157 **KANG, ELLEN S.; & GERALD, PARK S.** Hyperammonemia and Reye's syndrome. *New England Journal of Medicine*, 286(22):1216-1217, 1972. (Letter)

Transient hyperammonemia is one of the biochemical features of Reye's syndrome. The citrulline level in serum from 2 affected children was undetectable while other urea cycle intermediates (ornithine, aspartate, and arginine) were normal or slightly elevated. There is evidence that suggests inhibition of carbamyl phosphate synthetase or ornithine transcarbamylase. Hyperammoninemia is accompanied by a transient methylmalonyl-CoA racemase deficiency. (3 refs.) - *V. J. Goldberg.*

Children's Hospital Medical Center
Boston, Massachusetts

2158 **CROCKER, ALLEN C.** Plasma infusion therapy for Hurler's syndrome. *Pediatrics*, 50(5):683-685, 1972.

The effects of plasma infusion therapy for Hurler's syndrome are discussed in terms of possible therapy in various mucopolysaccharidosis syndromes. If it is assumed that most of the hereditary conditions can be attributed to a deficient specific lysosomal hydrolase activity, then replacement therapy would be the primal area for their treatment. In the instance of detailed studies with patients with Fabry's disease, it has been shown that large infusions of normal plasma can produce the appearance of transiently restituted ceramide-trihexosidase, but no useful clinical effects could be documented. The effects of plasma therapy in the various mucopolysaccharidoses are handicapped by the incomplete identification of relevant enzymatic parameters. Furthermore, the large volume plasma infusion trials currently being given to mucopolysaccharidosis patients would be too

small to provide enough factor for any notable amount of tissue effect. (10 refs.) - *A. C. Schenker.*

Children's Hospital Medical Center
Boston, Massachusetts

2159 **DEKABON, ANATOLE S.; HOLDEN, KENTON R.; & CONSTANTOPOULOS, GEORGE.** Effects of fresh plasma or whole blood transfusions on patients with various types of mucopolysaccharidosis. *Pediatrics,* 50(5):688-692, 1972.

Results of the effects of repeated transfusions of fresh normal plasma or whole blood to patients with mucopolysaccharidoses types I (Hurler), II (Hunter), and III (Sanfilippo) are presented. Clinical data on 5 patients with one of the 3 types of this disease all showed excretion of 5-10 times more urinary acid mucopolysaccharides (AMPS) than control patients of the same age; upon receiving plasma or blood transfusions, 2 of the patients with the Sanfilippo syndrome showed a slight decrease of urinary AMPS on the day of the transfusion and the following day or two. No noticeable clinical changes were observed in alertness, behavior, or mental or motor performance. In contrast to these findings, the administration of corticosteroids produced a significant and sustained reduction of urinary AMPS in these 2 patients. Although the results do not preclude the possibility of an increase in the deficient "factors" in the recipient of large quantities of whole blood or plasma, it is improbable that this would afford a sufficient change in the patient's metabolism of chondroitin sulfate B and heparin sulfate to be of therapeutic value. (212 refs.) - *A. C. Schenker.*

National Institutes of Health
Bethesda, Maryland 20014

2160 **YOUNG, ELISABETH; ELLIS, R. B.; & PATRICK, A. D.** Leukocyte beta-galactosidase activity in G$\mathcal{J}_1$-gangliosidosis. *Pediatrics,* 50(3):502, 1972. (Letter)

The results of 2 years of routine service assay of leukocyte beta-galactosidase activity are reviewed in connection with an article on this enzyme in the diagnosis of G$\mathcal{J}_1$-gangliosidosis. The range of enzyme activity for an all-age control group of 119 children and young adults was 99-393 (mean, 187). The activities of 6 patients (4 of whom were Maltese) with early infantile G$\mathcal{J}_1$-gangliosidosis were between 0 and 5.3, and that of a patient with late infantile form of this disease was undetectable. The activities of both parents from 2 families of patients with type 1 disease ranged from 66-89 (mean, 70). The assay of leukocyte beta-galactosidase provides a simple test for G$\mathcal{J}_1$-gangliosidosis. (2 refs.) - *A. C. Schenker.*

Institute of Child Health
Great Ormond Street
London, W.C.1, England

2161 **BAUM, DAVID; GUTHRIE, ROBERT; BRUNZELL, JOHN D.; VOGEL, WILLIAM C.; & BIERMAN, EDWIN L.** Triglyceride abnormality in infantile hypothyroidism. *American Journal of Diseases of Children,* 125(4):612-613, 1973.

An abnormality in lipid metabolism is reported in a 14-month-old boy with thyroid dysgenesis. Prior to therapy, triglyceride metabolism was abnormal as evidenced by elevated circulating triglyceride-rich pre-beta lipoproteins and increased plasma triglyceride concentration. With thyroxin therapy, the clinical manifestations of hypothyroidism and the laboratory values for assessment of thyroid activity became normal. The corrections of the lipid abnormalities were accomplished only after 20 weeks of therapy. The transient peak in postheparin lipase activity (PHLA) on all lipid substrates that occurred simultaneously with the elevation in triglyceride levels is difficult to explain. It may be that the enzyme synthesized during the earliest phase of thyroxin therapy is inactive against endogenous lipid substrate, that some other measure of PHLA is important in plasma triglyceride removal, or that triglyceride removal may be dependent upon factors in addition to lipoprotein lipase. (10 refs.) - *A. C. Schenker.*

Stanford University Medical School
Stanford, California 94305

2162 **SINGH, SARJIT; & *BRESNAN, MICHAEL J.** Menkes kinky-hair syndrome (trichopoliodystrophy): low cop-

per levels in the blood, hair, and urine. *American Journal of Diseases of Children*, 125(4):572-578, 1973.

Very low copper levels in blood, urine, and hair are reported in one case of kinky-hair syndrome, in addition to various EEG and roentgenographic abnormalities. Early onset of seizures, developmental regression, hair abnormalities, skeletal and blood vessel changes, and sex-linked recessive inheritance are described in a white, 5½-month-old boy. The absence of hematological changes, commonly seen in copper deficiency along with nutritional deficiency states, was noted in this case. In angiographic studies, marked tortuosity of the intracranial vessels and supernumerary branches was seen in both the anterior and posterior circulations; an aortogram demonstrated very tortuous renal, visceral, and femoral arteries and their peripheral branches. Poor intestinal absorption may be involved in this disease but has not been proven. (21 refs.) - *A. C. Schenker.*

300 Longwood Avenue
Boston, Massachusetts 02115

2163 **WALKER, W. ALLAN; LOWMAN, JAMES T.; & HONG, RICHARD A.** Measuring albumin turnover rates in patients with hypoproteinemia: a microtechnique. *American Journal of Diseases of Children*, 125(1):51-54, 1973.

A study designed to distinguish between hypoproteinemia due to decreased albumin synthesis and that due to excessive exogenous protein loss was conducted for further elucidation of the mechanisms which control homeostasis in patients with hypoproteinemia. Ten patients, aged 6 months to 15 years, were divided into: Group 1, the controls with no evidence of intrinsic liver disease or protein loss; Group 2, who were hypoalbuminemic with excessive protein loss; and Group 3, who were hypoproteinemic with severe liver disease. Each patient received an i.v. injection of selenomethionine Se 75; serum aliquots were obtained at various intervals following the injection; and Se 75 incorporation into endogenous albumin was determined. There was a rapid incorporation of the labeled amino acid into albumin in Group 2, reaching an earlier peak which was greater in albumin counts than in Group 3. The peak and time of radioactivity in Group 1 were intermediate between the other 2 groups. This technique may be used to evaluate the newborn infant or the severely malnourished child with hypoproteinemia. (26 refs.) - *A. C. Schenker.*

Massachusetts General Hospital
Boston, Massachusetts 02114

2164 **JOUNELA, A. J.; & KIVIMAKI, T.** Possible sensitivity to meperidine in phenylketonuria. *New England Journal of Medicine*, 288(26):1411, 1973. (Letter)

In connection with the interaction of meperidine with monoamine oxidase (MAO) inhibitors, as reported by Evans-Prosser, an alarming reaction in a mentally retarded patient with phenylketonuria is reported. A male homozygous 27-year-old patient was treated with L-dopa in doses of up to 100mg/kg daily to increase his activity. The treatment was stopped because it was not effective, and after a few weeks the MAO-inhibitor nialamide was administered at 2mg/kg daily. Sensitivity to meperidine, tested during that period for other purposes, caused increased motor activity, restlessness, gnawing movements, pallor, warm legs, and cyanosis around the mouth, with heart rate increased from 100 to 145 during the first 5 minutes; the test doses ranged from 0.2-0.4mg/kg. The symptoms disappeared within 2-3 hrs and nialamide treatment was then stopped. Treatment with nialamide seemed to potentiate the effects of meperidine. Animal experiments provide evidence for a mediator role by phenylethylamine in the monoamine-mediated excitation reactions after meperidine in phenelzine-treated animals. Phenylethylamine, a metabolite of phenylalanine, is a proper substrate for MAO, and in phenylketonuric patients might explain the observed reaction. (5 refs.) - *A. C. Schenker.*

Helsinki University Hospital
Helsinki, Finland

2165 **PERCY, ALAN K.** Antenatal detection of the sphingolipidoses. *New England Journal of Medicine*, 288(26):1405-1406, 1973.

The antenatal diagnosis of the disorders of sphingolipid metabolism, on the basis of enzymologic data, are discussed and the requisites that must be satisfied when genetic counseling is provided

are restated. These conditions require that the specific enzyme determination must be feasible in amniotic-fluid cells; that the affected fetus must be discriminated from the heterozygous or carrier fetus; and that when the pregnancy is terminated, the antenatal diagnosis must be confirmed in post-abortion tissues. When both parents can be identified as carriers of a specific disorder, the lack of effective treatment underscores the essential role of a program of antenatal detection. It is not now possible to detect all potential carriers for such disorders, so that additional affected persons can be anticipated. The techniques described by Leroy and his associates in still another fatal disorder in the group of sphingolipidoses, as well as those of other investigators, are generally available for the population at risk. (7 refs.) - *A. C. Schenker.*

2166 RAINE, D. N. Prevention: biochemical factors. In: Griffiths, Margaret I., ed. *The Young Retarded Child: Medical Aspects of Care.* Baltimore, Maryland, Williams & Wilkins, 1973, Chapter 17, p. 179-183.

Biochemical factors in the prevention of births or development of MR children are difficult to ascertain, especially in instances of enzyme deficiency. Inherited metabolic diseases of deficient enzyme origin are presently managed primarily by the unconstructive measure of abortion, with postnatal treatment still highly experimental. Heterozygote detection may be used to assess the risk of future afflictions, but suitable tolerances for recognition of metabolic diseases have not yet been well established. Guidance based on a likelihood ratio is more truthful, if not more helpful. With the development of specific methods for antenatal detection, births of infants with an enzyme deficiency disease may be avoided through therapeutic abortion. - *C. Wares.*

United Birmingham Hospitals
Birmingham, England

2167 KIHARA, HAYATO; VALENTE, MARIO; PORTER, MYNA T.; & FLUHARTY, ARVAN L. Hyperdibasicaminoaciduria in a mentally retarded homozygote with a peculiar response to phenothiazines. *Pediatrics,* 51(2):223-229, 1973.

Increased urinary excretion rates of the basic amino acids, lysine, arginine, and ornithine, are reported in a female MR patient with a history of adverse reactions to phenothiazines. Plasma concentrations of these amino acids were normal. The parents are first cousins, with further consanguinity on the mother's side. Consistent findings of massive lysinuria, argininuria, and ornithinuria were observed; cystine excretion was slightly elevated but excretion of other amino acids was within the normal range. Examination of urinary amino acids of both parents revealed excesses of the same amino acids, but to a lesser extent; cystine and other amino acids were not increased. Lysine excretion of 9 other members of the pedigree was also moderately elevated. It is submitted that the proband is homozygous for hyperdibasicaminoaciduria. The proband is initially studied because of her unusual reaction to drugs; the relation to the drugs may be a secondary manifestation of insult to cells of borderline metabolic competence. (13 refs.) - *A. C. Schenker.*

Pacific State Hospital
Pomona, California 91769

2168 Histidinaemia. *British Medical Journal,* 3(5824):431-432, 1972. (Editorial)

Some features of histidinemia, an inborn error of metabolism in which the amino acid histidine cannot be metabolized to urocanic acid due to the absence of histidase, are reviewed. Such cases were first discovered in the investigation of children with MR, but subsequent studies in the families of such children revealed that a number of normal children had this biochemical deficiency. In a review of 42 cases of histidinemia, 16 were completely normal and another 12 had an IQ in the low normal range, with behavior problems, seizures, or speech delay. Only 14 were MR: 6 of these had seizures, while 3 had an early infantile autism. Inherited histidinemia is an autosomal recessive condition, each parent carrying the gene and there being a 1-in-4 chance of any child having the disorder. It is not known whether a low histidine diet will change the prognosis for histidinemic children. (4 refs.) - *A. C. Schenker.*

2169 SIRISINHA, STITAYA; EDELMAN, ROBERT; SUSKIND, ROBERT;

CHARUPATANA, CHINDA; & OLSON, ROBERT E. Complement and C3-proactivator levels in children with protein-calorie malnutrition and effect of dietary treatment. *Lancet*, 1(7811):1016-1020, 1973.

The serum concentrations of individual complement proteins, including C1q, C1s, C3, C4, C5, C6, C8, and C9, and of C3 proactivator (C3PA) of 20 children with protein-calorie malnutrition were measured by radial immunodiffusion upon hospital admission and at intervals thereafter during varying dietary treatment and were compared with those of normal controls matched for CA and geographical location. The mean concentrations of 8 of the 9 complement components (except C4) measured on day 1 from 20 malnourished Ss were significantly lower than the mean of 19 controls ($p<0.05$), the 10 Ss with kwashiorkor showing lower mean levels than did the 10 Ss with marasmus. All 8 components in kwashiorkor Ss but only C5, C6, and C3PA in marasmic Ss were significantly lower than normal ($p<0.05$). All complement levels increased markedly when some Ss were placed on a high-calorie and high-protein diet, as compared with Ss who received high calorie and low protein. The study suggested that, regardless of the presence or absence of bacterial infection upon admission, complement levels of the various dietary groups were similar before dietary treatment and showed differences only after the diets were given. (27 refs.) - *B. J. Grylack.*

Mahidol University
Bangkok, Thailand

2170 SVENNINGSEN, N. W.; & LINDQUIST, B. Incidence of metabolic acidosis in term, preterm and small-for-gestational age infants in relation to dietary protein intake. *Acta Paediatrica Scandinavica*, 62(10):1-10, 1973.

Three groups of 334 term infants, 131 preterm infants, and 51 small-for-gestational age (SGA) infants each were divided into subgroups depending upon the amount of protein and solute content of the formula consumed and were investigated for the frequency of metabolic acidosis from day 5 to day 21 of postnatal life. After day 5, the incidence in each group was 4.79%, 20.61%, and 11.76%, respectively. The incidence among preterm (and appropriate-for-gestational age [AGA]) infants on a low-protein diet was 10.34%, and that among preterm (and AGA) infants on a high protein diet, 37.50%. An increase was also seen with increasing protein intake among SGA infants, but it was probably a function of gestational age rather than birthweight in this case. Thus, maturity is an important factor for the development of metabolic acidosis in the second and third week of life. (38 refs.) - *B. J. Grylack.*

University Hospital
S-221 85 Lund, Sweden

2171 REYNOLDS, E. H.; ROTHFELD, P.; & PINCUS, JONATHEN H. Neurological disease associated with folate deficiency. *British Medical Journal*, 2(5863):398-400, 1973.

Comparison of the neurologic status of 24 patients with severe folate deficiency in a general medical hospital population with that of an age- and sex-matched group of 21 patients without folate deficiency revealed a significant increase in the incidence of organic brain syndrome ($p<0.03$) and positive Babinski response ($p<0.03$) and a higher incidence of neuropathy in the folate-deficient patients. There was no evidence that anemia, significantly more prevalent in these patients, in itself influenced the neurologic findings. A higher incidence of neurologic disorders of all types was found in the folate-deficient alcoholics as compared with control alcoholics, but it did not reach significance. Cerebellar syndrome and neuropathy were more common in alcoholic than nonalcoholic folate-deficient patients, suggesting that the trend towards a higher incidence of neuropathy with folate deficiency may have been related more to alcoholism than to the deficiency alone. (17 refs.) - *B. J. Grylack.*

Yale University School of Medicine
New Haven, Connecticut 06510

2172 ITIABA, K.; BANFALVI, M.; CRAWHALL, J. C.; & MONGEAU, J.-G. Family studies of a Lesch-Nyhan patient from an isolated Canadian community. *American Journal of Human Genetics*, 25(2):134-140, 1973.

The finding of a child with the Lesch-Nyhan syndrome on Les Iles de la Madeleine, an isolated Canadian community in the gulf of the Saint Lawrence River, prompted a family study. The propositus, the seventh child of a family with 5 girls and with another boy who had no physical or mental abnormality, had 6 unaffected uncles, a factor which suggested that a new mutation had taken place. Cell selection studies with 6-thioguanine and 8-azaguanine indicated that the only heterozygotes among the patient's mother, youngest sister, aunt, and maternal grandmother were the mother and sister. These findings were corroborated by studies of ^{3}H-hypoxanthine incorporation into the fibroblast cells of the various Ss and into the cell nucleotides and derivatives. The possibility that the original cells grown in culture from the grandmother were not representative was not tested. However, laboratory indications that she was not a heterozygote female were supported by the evidence of her 6 unaffected male offspring. A new mutation probably occurred in an ovum of the maternal grandmother, who then gave birth to a daughter who was a heterozygote carrier for the syndrome. (13 refs.) - *B. J. Grylack.*

McGill University Clinic
Royal Victoria Hospital
Montreal, Quebec, Canada

2173 **ALTAY, CIGDEM; & SAY, BURHAN.** Three siblings with atypical mucopolysaccharidosis. *Acta Paediatrica Scandinavica*, 62(1):73-76, 1973.

A 10-year-old male, his 7-year-old sister, and his 5-year-old sister all excreted either heparin sulfate, dermatan sulfate, or both in the urine in excessive amounts and had specific bony changes without accompanying mental or physical retardation. Although their urinary excretion pattern, bony changes, and corneal clouding are characteristic of Hurler's syndrome, the absence of retardation makes it difficult to classify them as such. They probably represent atypical variants. (16 refs.) - *B. J. Grylack.*

Hacettepe Children's Hospital
Ankara, Turkey

2174 **EVANS, PHILIP.** Testing for Tay-Sachs heterozygotes. *Lancet*, 2(7825):391, 1973. (Letter)

Tay-Sachs carriers can now be detected, since their blood contains amounts of hexosaminidase A which lie between those of affected infants and of noncarriers. Inasmuch as the carrier state is 10 times as common among Ashkenazi Jews as it is in the population at large, a testing program for Jews is warranted. A laboratory has been set up for such testing that will visit groups to obtain blood specimens or will test individuals by appointment at the hospital. - *B. J. Grylack.*

British Tay-Sachs Foundation
Hospital for Sick Children
Great Ormond Street
London WC1N 3JH, England

2175 **SCHONBERG, D.** Plasma growth hormone in cerebral gigantism, Laurence-Moon-Bardet-Biedl syndrome, Bloom syndrome and in Fanconi anemia. *Acta Paediatrica Scandinavica*, 62(1):111-112, 1973. (Abstract)

Growth hormone (GH) in plasma was measured under various conditions with a modified double antibody technique. The response of GH to insulin-induced hypoglycemia was normal in 3 children with cerebral gigantism, but maximal stimulation after arginine infusion was subnormal in 2 cases (4.1 and 3.9ng/ml, respectively). One of 2 children with Laurence-Moon-Bardet-Biedl syndrome had normal height for CA and showed a normal response of GH to insulin-induced hypoglycemia, while the other child with retarded growth responded subnormally to arginine (3.3ng/ml). One child with Bloom syndrome had a subnormal rise to insulin with a late rise of GH to 14ng/ml after 210 min, and the nitrogen retention test was subnormal. GH therapy appears to have had a favorable effect on growth and hemopoiesis in a girl with Fanconi anemia and severe growth retardation whose GH stimulation was in the range of hypopituitary dwarfs. - *B. J. Grylack.*

2176 **BARTOSOCAS, CHRISTOS S.; PAPASOTIRIOU, NIKI; KARAGEORGA, MARKESIA; & MOSER, HUGO W.** Hunter's syndrome and Cooley's anaemia in the same patient: effect of multiple

transfusions. *Acta Paediatrica Scandinavica*, 62(1):66-68, 1973.

A 5-year-old boy with Hunter's syndrome and Cooley's anemia has received 38 fresh frozen plasma transfusions during the last 4 years. Morphologically the propositus presented only the features of a mucopolysaccharidosis. Cooley's anemia was evidenced by splenomegaly, skull thickening, and osteoporotic lesions of the skeleton. Whatever changes the transfusions may have produced in the mucopolysaccharidosis were insufficient to be recognized clearly, and the development of phenotypic changes typical of the Hunter syndrome was not prevented. (5 refs.) - *B. J. Grylack.*

3 Kapsali Street
Athens 138, Greece

2177 **WATERLOW, J. C.** Note on the assessment and classification of protein-energy malnutrition in children. *Lancet*, 2(7820):87-89, 1973.

The importance of an international system for the estimation and classification of milk protein-energy malnutrition is discussed. The most commonly used method of assessment is based on deficit on weight-for-age; this assessment, however, may represent 2 quite distinct conditions: type A, in which there is a deficit in weight-for-height (wasting), and type B, in which there is a deficit in height-for-age (stunting). In practice, in a great many undernourished children both processes are present and there is a mixture of acute and chronic and of present and past undernutrition. If one is dealing with a population which is genetically small, the interpretation of the results could be adjusted, as for example, calling grade 1 normal, grade 2 mild, etc. It seems reasonable to suppose that wasting and stunting have different histories, perhaps related to different dietary backgrounds and possibly different sequelae; these have to be distinguished before their practical importance can be assessed. (19 refs.) - *A. C. Schenker.*

London School of Hygiene and Tropical Medicine
London WC1, England

2178 **DEOL, M. S.** Congenital deafness and hypothyroidism. *Lancet*, 2(7820):105-106, 1973. (Letter)

The effects of induced hypothyroidism on hearing were investigated in mice, which have an organ of Corti almost identical to that of man. Mice of the inbred strain C57BL/Gr were given 0.1% propylthiouracil (PTU) in drinking water. Their offspring showed severe loss of hearing, invariably associated with abnormalities in the organ of Corti. These abnormalities were increasingly milder when the treatment was begun at progressively later stages after the onset of pregnancy. When sodium-L-thyroxine was added to the drinking water containing PTU, both the hearing and the organ of Corti in the offspring were normal. The findings are of clinical interest because hyperthyroid women are sometimes treated with thiouracil during pregnancy. They may also prove of some value in the prevention or mitigation of deafness in cases of sporadic hypothyroidism and Pendred's syndrome, which is caused by a recessive gene. (5 refs.) - *A. C. Schenker.*

University College London
London, England

2179 **SHENKMAN, L.; MITSUMA, T.; PENNA, M.; MEDEIROS-NETO, G. A.; MONTEIRO, K.; PUPO, A. A.; & HOLLANDER, C. S.** Evidence for hypothyroidism in endemic cretinism in Brazil. *Lancet*, 2(7820):67-69, 1973.

The etiology of the neurological form of endemic cretinism was studied in 12 cretins from the midwest region of Brazil, an area where endemic goiter and endemic cretinism are common. Eleven patients (7 women and 5 men) had grade II or III multinodular goiters and one had grade I goiter. Six had severe impairment of mental function; 6 showed only a moderate degree of mental deficiency; 9 were deaf-mutes. Thyroid function was in keeping with the clinical impression of euthyroidism. The mean serum protein-bound iodine was 5.5 microgm/100ml and the mean 24-hour thyroidal uptake of ^{131}I was 32.6. Three patients had total and free thyroxine levels slightly below normal; 6 had raised basal thyrotrophin levels; 5 had increased thyrotrophin response to thyrotrophin-releasing hormone; and 6 had a decreased response to this hormone. The demonstration that cretins have evidence of thyroidal failure may support the view that these

patients were, in fact, hypothyroid during a critical stage of their development, resulting in irreversible neurologic damage. (20 refs.) - *A. C. Schenker.*

New York University School of Medicine
New York, New York 10016

2180 **WHITEHEAD, R. G.; COWARD, W. A.; & LUNN, P. G.** Serum-albumin concentration and the onset of kwashiorkor. *Lancet*, 1(7794):63-66, 1973.

The value and clinical significance of serum-albumin measurements as an indication of the onset of the critical phase of kwashiorkor are described in an investigation of 326 children. Serum measurements included: albumin, beta-lipoprotein, valine, alanine, cortisol, insulin, growth hormone, and colloidal osmotic pressure. Except for the amino acids and insulin, there was no major change while serum-albumin concentration was falling to 3.0gm/100ml, but below this value all the measurements were affected simultaneously, showing a distinct deviation towards the pattern found in severe kwashiorkor. This indicates that at the same time as the child is becoming more susceptible to edema, he is also becoming more susceptible to the development of a fatty liver. If measurements are to be used in the detection of a malnourished child, the system described for assessing the significance of albumin should be adaptable to most other measurements. (22 refs.) - *A. C. Schenker.*

Medical Research Council Child Nutrition Unit
Kampala, Uganda

2181 **GIBBERD, MARGARET G.; & STAFFURTH, J. S.** Oxprenolol in thyrotoxicosis. *Lancet*, 1(7796):205, 1973. (Letter)

A clinical trial with 40mg oxprenolol t.i.d. administered to outpatients with moderately severe thyrotoxicosis is reported. The drug was compared with placebo tablets on a double blind basis in 16 patients. More patients preferred the placebo tablets; the clinicians gave a preference for oxprenolol in 4 Ss compared with 1 for placebo, but the response was not striking; in 11 instances no preference was given by the physicians. It is suggested that oxprenolol failed to control the symptoms of thyrotoxicosis because this drug has some inherent sympatheticomimetic activity. (2 refs.) - *A. C. Schenker.*

Lewisham Hospital
London SE13 6LH, England

2182 **OCKERMAN, PER-ARNE; AUTIO, SEPPO; & NORDEN, NILS E.** Diagnosis of mannosidosis. *Lancet*, 1(7796):207-208, 1973. (Letter)

On the basis of the correct diagnosis of the new storage disease mannosidosis in 5 patients, certain findings are submitted which should be helpful in the diagnosis of this disease. Symptoms and signs comprised: progressive psychomotor retardation, coarse facies, corneal or lenticular opacities, and slight hepatosplenomegaly. The morphology included: vacuolized lymphocytes, and lysosomal storage phenomena in tissue biopsies under electron microscopy. A carbohydrate assay revealed large amounts of mannose-containing oligosaccharides in the urine and in liver tissue. Enzyme activities demonstrated low alpha-mannosidase activity in liver and white blood cells. (5 refs.) - *A. C. Schenker.*

University Hospital
Lund, Sweden

2183 **STOKKE, ODDVAR; ELDJARN, LORENTZ; JELLUM, EGIL; PANDE, HELENE; & WAALER, PER ERIK.** Beta-methylcrotonyl-CoA carboxylase deficiency: a new metabolic error in leucine degradation. *Pediatrics*, 49(5):726-735, 1972.

A 4½-month-old girl with closely consanguineous parents was shown by gas-liquid chromatography to be excreting 2 abnormal organic acids, β-hydroxyisovaleric acid and β-methylcrotonylglycine, in amounts of about 400mg and 100mg per 24 hours, respectively. The latter compound has not been found previously in human material. The proposita manifested a clinical picture similar to the early-presenting type of infantile progressive spinal muscular atrophy (Werdnig-Hoffmann's disease). The peculiar smell from her urine suggested the possibility of a metabolic disorder. A low-leucine diet led to an immediate reduction of the abnormal urinary metabolites and to the disappearance of the

unpleasant smell, but no clinical improvement was seen. The defect in this patient was probably caused by a failure in the β-methylcrotonyl-CoA carboxylase step in the degradation pathway of leucine. (13 refs.) - *B. J. Grylack.*

Institute of Clinical Biochemistry
Rikshospitalet
Oslo 1, Norway

2184 **MEDEIROS-NETO, GERALDO A.; BLOISE, WALTER; & ULHOA-CINTRA, A. B.** Partial defect of iodide trapping mechanism in two siblings with congenital goiter and hypothyroidism. *Journal of Clinical Endocrinology and Metabolism*, 35(3):370-377, 1972.

A 23-year-old female and her 34-year-old brother, both with congenital goiter and hypothyroidism, presented evidence of a partial defect in the iodide trapping mechanism in the thyroid, salivary glands, and gastric mucosa. The parents were cousins once removed. Both Ss demonstrated a low basal metabolic rate, high cholesterol level, negative tanned red cell agglutination test for antithyroglobulin antibodies, and a very low protein-bound iodine, with serum thyroxine iodines of 1.0 and 1.8 μg/100 ml, respectively. Plasma chromatography of iodinated compounds revealed only iodide and iodoproteins. The ratios for saliva/plasma and gastric fluid/plasma were above unity but were lower than those of normal Ss without thyroid disease. Repetition of testing for these ratios following tri-iodothyronine treatment showed no improvement. The defective iodide trapping seemed to lead to a state of considerable iodine deficiency within the gland. The defect is apparently due to a recessive factor, affecting 2 siblings in 1 generation. (13 refs.) - *B. J. Grylack.*

Hospital das Clinicas
University of Sao Paulo Medical School
Sao Paulo, Brazil

2185 **SAMUEL, A. M.; & DESHPANDE, U. R.** Growth hormone levels in protein calorie malnutrition. *Journal of Clinical Endocrinology and Metabolism*, 35(5):863-867, 1972.

The secretion of human growth hormone was studied in 54 children aged 4 months to 5 years suffering from marasmus and 30 normal children matched for CA, sex, and socioeconomic status. The mean normal level was 2.02 SD ± 1.7ng/ml (upper range of normal at 5.5ng/ml + 2 SD) as compared with a mean of 7.24ng/ml ± 8.4 SD in marasmus, a difference significant at $p < .017$. Correlations were found between growth hormone levels and severity of the disease and between fasting blood sugar levels and fasting growth hormone levels. The data did not support the conjecture that protein depletion would lower the secretion of growth hormone levels. Growth hormone levels were raised above normal levels in children who were more severely hypoalbuminemic; this rise was not so apparent when albumin levels were above 2.5g/100ml, but the correlation between serum albumin levels and growth hormone levels ($r=0.3$, $p<0.05$) was poor, nonetheless. Dietary replacement of proteins over a 6-week period effectively lowered the growth hormone levels in 75% of the children studied; serum albumin levels improved and fasting blood sugar levels were normal. A significant response of growth hormone levels in 3 of 11 patients to insulin-induced hypoglycemia contrasted with nonresponsiveness in the remaining 8, although replacement of high protein diet for 4 to 6 weeks caused the return of a positive response. (18 refs.) - *B. J. Grylack.*

Bhabha Atomic Research Center
Tata Memorial Hospital
Parel, Bombay-12, India

2186 **LEVINE, SEYMOUR; & HOENIG, EUGENE M.** Astrocytic gliosis of vascular adventitia and arachnoid membrane in infantile Gaucher's disease. *Journal of Neuropathology and Experimental Neurology*, 31(1):147-154, 1972.

Infiltration of Gaucher cells was accompanied by astrocytic gliosis in a 6-year-old Negro male who had been ill since infancy. Fibroglial tissue was unusual in its abundance and in its location in vascular adventitia and meninges. In no case was fibroglial tissue observed without Gaucher cells, indicating that the Gaucher cells initiated the lesions in this patient. The astrocytes may have required years to respond and invade the lesions. The fibroglial tissue in the arachnoid was in continuity with and probably derived from the parenchymal glia through breaks in the pia, and

the fibroglial tissue in the veins, also in continuity with parenchymal glia, may have transgressed the limiting glial membrane and invaded the vessels in this way. The presence of astrocytic fibers surrounded by myelin was a rare finding. The unique nature of the lesions in this patient may have been due to his unusually long survival. (18 refs.) - *B. J. Grylack.*

New York Medical College Center for
Chronic Disease
New York, New York 10017

2187 **WELSH, JACK D.; & LANGDON, DAVID E.** Lactose to treat hepatic encephalopathy in patient with lactose malabsorption. *New England Journal of Medicine*, 286(8):436, 1972. (Letter)

Preliminary observations are reported on the treatment of hepatic encephalopathy with oral lactose. Lactulose metabolism by bacteria causes an acid pH in the colon resulting in a decrease of absorbable ammonia (NH_3). and an increase in nonabsorbable ammonia ions (NH_4). Since a large number of Americans have primary lactose malabsorption, lactose was substituted for lactulose in the treatment of 3 American Indians and 1 Mexican-American with hepatic encephalopathy. The diagnosis of lactose malabsorption was made by a lactose tolerance test (in 1 patient) and by the presence of acid diarrhea with reducing substances in the stool after lactose ingestion in the other 3 patients. All the patients responded well to 150 gm of lactose daily. (3 refs.) - *A. C. Schenker.*

University of Oklahoma
Health Sciences Center
Oklahoma City, Oklahoma

2188 **SUGITA, MUTSUMI; DULANEY, JOHN T.; & MOSER, HUGO W.** Ceramidase deficiency in Farber's disease (lipogranulomatosis). *Science*, 178(4065):1100-1102, 1972.

Ceramidase activity in Farber's disease (lipogranulomatosis) was examined in the stored postmortem tissues of a 9-month-old girl with this disease. No ceramidase activity was detected in the kidney or cerebellum of this patient; storage of tissues at -60 C for periods up to 11 years has no marked effect on the activities of the control enzymes. A specific inhibitor of ceramidase is absent in Farber's tissue. The demonstrated accumulation of ceramide in 2 patients with Farber's disease, coupled with the deficiency of ceramidase activity in the patient described, suggests that a genetically determined defect in ceramide degradation forms the biochemical basis for this disorder. The finding of an activity below 0.02 nmole of ceramide synthetase in the kidney of the patient with Farber's disease, in contrast to 6 patients without Farber's disease who had a specific activity of 1.44-2.58 nmole, suggests a possible new pathway to be considered in the biosynthesis of ceramide. (18 refs.) - *A. C. Schenker.*

Eunice Kennedy Shriver Center
Walter E. Fernald State School
Waverley, Massachusetts 02178

2189 **O'GRADY, D. J.; MULHERN, T.; & BERRY, H. K.** Normal IQ distributions of early-treated phenylketonuric children and their unaffected siblings: failure to replicate a trimodal response or negative skew. *Nature*, 238(5360):169-170, 1972.

Data collected on phenylketonuric (PKU) children were analyzed to test the contention by Fuller and Schuman that PKU is not based on a single gene defect as is generally accepted. According to these authors, a trimodal frequency distribution of IQs is representative of early and late treated PKUs. Fuller also reported a negative skew in the IQ of unaffected siblings of PKU children; additional data are presented on such Ss. The early treated children used in this analysis obtained from Hudson's data were treated before the age of 4 months, and only cases on diet at time of last testing (with Stanford-Binet Intelligence Scale for <2-year-olds) were included for analysis (61 cases). The IQs of normal or unaffected siblings of PKU children analyzed were also taken from Hudson's data (70 cases). Statistical analysis showed the IQ distribution of the 61 cases to be normal. Frequency distributions of IQs for Hudson's early treated cases and for Fuller's 26 early treated cases (N = 87) combined show Fuller's apparent bimodal distribution to diminish considerably. Differences in evaluation are attributed to differences in sampling. The data presented indicate normal IQ distribution in the early treated PKU cases and

unaffected siblings; these data are consistent with a single gene defect in PKU. (7 refs.) - *A. C. Schenker.*

Children's Hospital Research Foundation
Cincinnati, Ohio

2190 **JOSE, DAVID G.; & GOOD, ROBERT A.** Immune resistance and malnutrition. *Lancet*, 1(7745):314, 1972. (Letter)

Analysis of the influence of protein-calorie malnutrition upon humoral and cellular immune responses has shed new light on the long-term implications of early nutritional status. Measurements of cellular and humoral immune responses to tumor antigens demonstrated depression of hemagglutinating, cytotoxic, and blocking antibody titers after primary immunization in mice fed diets of less than 10% protein-calories. Cytotoxic cell-mediated immunity, as measured by *in vitro* assay, remained intact in animals fed 5% protein-calories but was depressed in those fed 3% protein diets. Lack of humoral antagonism of cellular immune surveillance may be responsible for the striking reduction in incidence and restricted spread of malignant tumors in undernourished animals. The long-term retardation of normal growth and maturation, leading to depression of cell number and intellectual brain function in animals and man which results from severe nutritional deprivation in early infancy, may be paralleled by a long-term effect upon the developing immunological system in man. Severe kwashiorkor with an early onset has been associated with profound depression of total serum-immunoglobulin levels and immunological defects, components of which persisted after refeeding. (7 refs.) - *B. J. Grylack.*

Research Laboratories of the
Variety Club Heart Hospital
University of Minnesota
Minneapolis, Minnesota 55455

2191 **ADLARD, B. P. F.; & DOBBING, JOHN.** Vulnerability of developing brain. V. Effects of fetal and postnatal undernutrition on regional brain enzyme activities in three-week-old rats. *Pediatric Research*, 6(1):38-42, 1972.

Enzyme activity of crude mitochondrial acetylcholinesterase (EC) was used as a measure of activity in nerve endings in 4 brain areas in normal and undernourished 3-week-old rats (hooded strain). Undernourished dams were given the same food as the controls but the quantity was restricted to about 50% of the food intake of the controls; this was begun on the seventh day of gestation. A total of 5 control and 5 undernourished litters (reduced to 4 males and 4 females) were reared to 21 days. Crude mitochondrial EC was assayed in the brains of 4 animals from each litter; areas investigated were brain stem, cerebellum, forebrain, and olfactory lobes. Results revealed significant deficits in crude mitochondrial EC activity in the forebrain, brainstem, and olfactory lobes of undernourished animals compared with controls ($p<0.001$), when expressed in terms of tissue dry weight. When expressed in terms of wet weight, differences between undernourished and control animals were found only for fumarate hydratase and 5′-nucleotidase activity. In the undernourished animals, fumarate hydratase was higher per gram dry weight, and 5′-nucleotidase activity was higher in both dry and wet weight, as well as in tissue protein. The results reveal that undernutrition in early life may affect enzymic composition in the young rat and may be responsible for growth retardation. (20 refs.) - *A. C. Schenker.*

University of Manchester
Clinical Science Building
Manchester 13, England

2192 **SEASHORE, MARGRETTA R.; DURANT, JOSEPH L.; & *ROSENBERG, LEON E.** Studies of the mechanism of pyridoxine-response homocystinuria. *Pediatrics Research*, 6(3):187-196, 1972.

The effect of pyridoxine administration on plasma and urinary amino acid concentrations and urinary inorganic sulfate excretion was studied during normal dietary intake and under methionine loading, in order to elucidate the nature of pyridoxine-responsive homocystinuria. Two young men (ages 16 and 18 years) with known homocystinuria were studied. A dose-dependent response to pyridoxine was noted when graded doses (12.5-500mg) were given; plasma methionine was in the normal range in both patients at a pyridoxine dose of 12.5mg; however, whereas one patient required only

25mg pyridoxine per day for correction of plasma methionine, homocystine, and cystine concentrations, the other patient required more than 50mg pyridoxine per day. Amino acid excretion also differed markedly in the two patients during methionine loading. Under basal conditions, synthase activity was less than 5% of normal in both patients, but addition of saturating concentration of pyridoxal phosphate to the assay mixture of the cultured skin fibroblasts stimulated synthase activity to different degrees in the two Ss. The difference in responsiveness, both in vivo and in vitro, may be mediated by simulation of defective cystathionine synthase activity in one patient and by enhancement of alternative pathways of sulfur amino acid metabolism in the other patient. (35 refs.) - *A. C. Schenker.*

Yale University School of Medicine
New Haven, Connecticut 06510

2193 **CRAWHALL, J. C.; HENDERSON, J. F.; & KELLEY W. N.** Diagnosis and treatment of the Lesch-Nyhan syndrome. *Pediatrics Research*, 6(5):504-513, 1972.

The Lesch-Nyhan syndrome, characterized by marked hyperuricemia, excessive uric acid production, choreathetosis, striking MR and growth retardation, spasticity and self-mutilation, is reviewed in terms of the chemical basis for the disease, its diagnosis and treatment. The enzyme defect in this syndrome is the lack of hypoxanthine-guanine phosphoribosyltransferase (HGPRT) which catalyzes the conversion of hypoxanthine to inosinic acid and guanine to guanylic acid in the presence of phosphoribosylpyrophosphate (PP-ribose-P). Preliminary studies suggest that one factor which regulates HGPRT in brain slices is the availability of PP-ribose-P; although the potential importance of HGPRT activity in brain is suggested, the origin of guanine is not known. Since the syndrome was first described in 1964, about 80 cases have been reported, but the incidence of this disease in any population cannot be estimated accurately. The metabolic defect in a male fetus can now be determined by prenatal diagnosis. After birth, male infants may be diagnosed by an elevated urinary uric acid:creatinine ratio. Treatment is only effective in the case of hyperuricemia associated with gouty arthritis and hyperuricemic nephropathy. (72 refs.) - *A. C. Schenker.*

4 Main, Royal Victoria Hospital
Montreal 112, Quebec, Canada

2194 **CONRAD, GARY W.; SHERMAN, DEBRA; & *DORFMAN, ALBERT.** An ultrastructural comparison of normal and Hurler syndrome dermal fibroblasts. *Pediatrics Research*, 6(6):563-575, 1972.

Electron microscope studies of dermal fibroblasts from 3 patients with Hurler's syndrome were studied, because of their role in biosynthesis of polysaccharide. Specimens of skin from the 3 patients and from 3 normal control Ss were obtained from the deltoid region. Fibroblast cultures, established from these samples, were grown under 10% CO_2-90% air in modified Eagle's medium which contained 50 mM $NaHCO_3$, 0.57 mM ascorbic acid, and 10% fetal calf serum. Cells were incubated for varying lengths of time in nutrient medium containing colloidal gold, incubated to localize acid phosphatase and aryl sulfatase B activities histochemically, and assayed for these enzymes biochemically. Normal fibroblasts could be consistently distinguished from Hurler cells during any stage of the culture cycle by the criteria of vacuole number and Golgi morphology. The greatest difference observed in cell morphology derived from the Hurler mutation. The cytoplasm of typical normal fibroblasts contained only about one-tenth as many vacuoles as did typical Hurler fibroblasts. Hurler cells contained granules which stained metachromatically with toluidine blue. Aryl sulfatase B activity and acid phosphatase activity were found in the occasional large cytoplasmic vacuoles and residual bodies of normal fibroblasts, but were absent from Hurler cells. The vacuoles seen in normal and Hurler fibroblasts seem to be secondary lysosomes, because they contain both extracellular and intracellular material. (40 refs.) - *A. C. Schenker.*

University of Chicago (Pediatrics)
Chicago, Illinois 60637

2195 **OKADA, SHINTARO; MCCREA, MARY; & *O'BRIEN, JOHN S.** Sandhoff's disease (GM_2 gangliosidosis Type 2): clinical, chemical, and enzyme studies in five patients. *Pediatrics Research*, 6(7):606-615, 1972.

Five patients with Sandhoff's disease are

described and clinical features are compared with those of Tay-Sachs; differences between serum hexosaminidase A and B in the two diseases are discussed. The 5 patients presented are from 3 non-Jewish families. Clinical features of Sandhoff's disease are summarized for 7 patients (2 patients from other reports) and include: onset of motor weakness between 6 and 8 months of age; fatality between the second and third year of life; presence of cherry red spots in the macular region of all patients; and progressive macrocephaly, present after 12 months of life, in several patients. MR and seizures may also occur in Sandhoff's disease. The simplest means for differentiation between Tay-Sachs and Sandhoff's diseases is the hexosaminidase assay; whereas in Tay-Sachs disease hexosaminidase A is deficient, both A and B hexosaminidase are deficient in Sandhoff's disease. The prenatal diagnosis of the latter is now possible by means of midpregnancy amniocentesis. It is suggested that a number of non-Jewish cases of Sandhoff's have been erroneously diagnosed as Tay-Sachs. (28 refs.) - *A. C. Schenker.*

University of California at San Diego
La Jolla, California 92037

2196 **WADA, Y.; *TADA, K.; TAKADA, G.; OMURA, K.; YOSHIDA, T.; KUNIYA, T.; AOYAMA, T.; HAKUI, T.; & HARADA, S.** Hyperglycinemia associated with hyperammonemia: in vitro glycine cleavage in liver. *Pediatrics Research*, 6(7):622-625, 1972.

Biochemical studies on a patient with nonketotic hyperglycinemia associated with hyperammonemia are presented. A liver specimen, obtained by surgical biopsy, was analyzed and a control liver specimen was used as reference. Glycine and ammonia plasma levels, at time of biopsy, were 8.28mg/100ml and 195microg/100ml, respectively. Glycine cleavage and serine hydroxymethylase were determined in liver homogenate; activity of the urea cycle enzymes was assayed by the procedure of Brown and Cohen. The results revealed that $^{14}CO_2$ formation from glycine-1-^{14}C was extremely low in the patient's liver compared with the normal liver. The incorporation of ^{14}C from glycine-1-^{14}C and glycine-2-^{14}C into serine was about equal in the patient's liver; in the control, the ^{14}C-serine formed from glycine-2-^{14}C was about twice the amount formed from glycine-1-^{14}C. These findings indicated defective glycine cleavage in the patient. The activities of the urea cycle enzymes were found to be normal in the patient's liver. There is a possibility that accumulation of glycine or its metabolites may inhibit the activity of the urea cycle or that accumulated glycine is converted to glyoxylate by glycine oxidase to release ammonia. (29 refs.) - *A. C. Schenker.*

Department of Pediatrics
Osaka City University
School of Medicine
Abeno-Ku, Osaka, Japan

2197 **SCOTT-EMUAKPOR, A.; HIGGINS, J. V.; & *KOHRMAN, A. F.** Citrullinemia: a new case, with implications concerning adaptation to defective urea synthesis. *Pediatrics Research*, 6(7):626-633, 1972.

A 33-year-old MR male with citrullinemia is described; the deficiency of argininosuccinate synthetase was presumably responsible for this condition. The patient was able to synthesize normal amounts of urea under ordinary dietary conditions. A low protein diet, a normal diet, and a high protein diet with and without milk were administered at different times and serum and 24-hr urine specimens were collected over 3 weeks of testing. Amino acid determinations were performed by ion exchange chromatography; serum ammonia was determined by microdiffusion and a colorimetric method by Conway and Caraway, respectively; colorimetric methods were used for creatinine determination; and enzymatic studies of cultured fibroblasts were conducted in another laboratory. Excretion of urea was reduced on the low protein diet and rose on the high protein diet; the increase in the latter was not proportional to the large amounts of ingested nitrogen, suggesting a limited response to high protein. Daily excretions of citrulline, homocitrulline, and homoarginine were very high on the high protein diet. There was an absence of ammonia intoxication and the ability to synthesize normal amounts of urea was observed. Skin fibroblast cultures showed deficient activity of argininosuccinate synthetase. It is postulated that as the patient becomes older he may adapt to a block in the usual pathways of urea synthesis by development of an alternate mechanism of ammonia disposal. (24 refs.) - *A. C. Schenker.*

Department of Human Development
Michigan State University
East Lansing, Michigan 48823

2198 SCHNEIDER, EDWARD L.; ELLIS, WILLIAM G.; BRADY, ROSCOE O., MCCULLOCH, JOHN R.; & *EPSTEIN, CHARLES J. Prenatal Niemann-Pick disease: biochemical and histologic examination of a 19-gestational week fetus. *Pediatrics Research*, 6(9):720-729, 1972.

Biochemical and morphologic data on a 19-gestational-week fetus with Niemann-Pick disease (NPD) are presented. Liver, spleen, and brain tissues from the NPD fetus and age-matched control fetuses were analyzed for sphingomyelinase activity at pH 5.0 and glucocerebrosidase was measured at pH 6.0; thin-layer chromatography was used for quantitative measurements of the sphingomyelin extracted from NPD fetal liver. A deficiency of sphingomyelinase activity in liver and brain and increase in sphingomyelin content of liver, together with a positive family history, confirmed the diagnosis of NPD. Morphological findings included: cellular enlargement with cytoplasmic vacuolization and eccentric nuclei on light microscopy; increased deposition of phospholipids; and increased acid phosphatase reaction product. On electron microscopy, liquid cytosomes were observed in the liver, spleen, cerebral vessels, and occasional neurons. It is suggested that the primary defect in NPD is limited to sphingomyelin catabolism and that the increased levels of cholesterol seen later in the disease may be secondary to the disordered sphingolipid metabolism. Genetic counseling, detection of heterozygote carriers, and prenatal diagnosis by examination of cultured amniotic cells are recommended for the prevention of this hereditary disorder. (39 refs.) - *A. C. Schenker.*

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San Francisco, California 94122

2199 LESTER, R.; HILL, M. W.; & BANGHAM, A. D. Molecular mechanism of Tay-Sachs disease. *Nature*, 236(5340):32-33, 1972.

A model to explain the mechanism underlying Tay-Sachs disease is presented, using the interactions of gangliosides with phosphatidyl choline (lecithin) in various proportions. "Myelins" formed from a mixture of the two molecules showed wide lamellar spacings when compared with those formed from lecithin alone. The results showed that at relative concentrations of ganglioside less than 30%, more than 95% of the total lipid sedimented, the pellet being in the form of a smectic mesophase. At relative concentrations of ganglioside of more than 65%, most of the lecithin was in the supernatant phase; at concentrations between 30 and 65%, both a lipid-containing supernatant and a pellet were observed. It is suggested that, if the model reflects conditions *in vivo*, the lamellar membranous cytoplasmic bodies, composed of 20-50% ganglioside mixed with lipids and protein which fill the cytoplasm of ganglion cells in Tay-Sachs disease, form by similar processes as those in synthetic mixtures of ganglioside-lecithin containing 0-65% ganglioside. (8 refs.) - *A. C. Schenker.*

Boston University School of Medicine
Boston, Massachusetts

2200 TERPLAN, KORNEL L.; & CARES, HERBERT L. Histopathology of the nervous system in carnosinase enzyme deficiency with mental retardation. *Neurology*, 22(6):644-655, 1972.

The clinical history of 2 retarded siblings is reported, in whom increased amounts of carnosine were found in the urine and an elevated carnosine concentration in the serum, observed in the course of their physical and mental deterioration; this was associated with a deficiency of serum carnosinase. Following a normal birth, the 2 male siblings had seizures between 2 and 4 months of age, followed by progressive mental impairment within the first 2 years and physical impairment from the third year on. The older boy died at age 7.5 years; postmortem examination revealed marked emaciation with flexion deformities; histological findings showed distinct degenerative changes in peripheral nerves with severe axonal degeneration; fusiform swellings and spiral and fragmented segments; distinct demyelination, fibrosis, and edema of the brachial plexus nerve; extensive liquefaction necrosis of muscle fibers; and complete absence of Purkinje cells in the cerebellum and proliferation of Bergmann cells; neuronal loss in cortex,

most marked in occipital and motor areas; and only slight loss of neurons in basal ganglia. Although the familial occurrence of infantile neuroaxonal dystrophy points to a genetically determined metabolic disorder, with an inherited enzyme deficiency, the specific nature of such defect has not been established. The association of neuroaxonal dystrophy with carnosinase enzyme deficiency in these cases should stimulate further research in this connection. (14 refs.) - *A. C. Schenker.*

Children's Hospital
Buffalo, New York 14222

2201 **ROSMAN, N. PAUL; MALONE, MICHAEL J.; HELFENSTEIN, MYRNA; & KRAFT, EDITH.** The effect of thyroid deficiency on myelination of brain: a morphological and biochemical study. *Neurology*, 22(1):99-106, 1972.

Biochemical and morphological changes in neonatal hypothyroidism in Sprague-Dawley white rats are reported. Female rats received at midterm or near term of pregnancy an iodine-free diet; within 24 hours after birth, half of the pups of each litter (12-15 pups per litter) were radiothyroidectomized; the remaining pups were injected i.p. with 0.05ml normal saline. The rats injected with radioiodine were seen to be rendered hypothyroid as evidenced by total destruction of thyroid tissue. Neonatal hypothyroidism retarded body growth, with cessation of overall weight gain after 3-4 weeks of age. Histologically, a 3-6-day delay of myelination occurred in all tracts in brains of hypothyroid rats from 14 days of age. These changes correlated well with reduction in proteolipid and lipid hexose in brain. The accumulation of lipid hexose in developing brains of hypothyroid rats was more delayed than that of the lipid-soluble protein. The basic protein fraction, bound mainly by ionic bonds with acidic lipids or proteins, is viewed as the structural feature of a template upon which myelin lipids are oriented. A selective effect of neonatal hypothyroidism on the formation of basic proteins is postulated. (34 refs.) - *A. C. Schenker.*

Boston City Hospital
Boston, Massachusetts 02118

2202 **WATERLOW, J. C.** Classification and definition of protein-calorie malnutrition. *British Medical Journal*, 3(5826):566-569, 1972.

An accepted classification and definition of protein-calorie malnutrition is needed so that all studies of prevalence will use the same criteria and in order that the planning of preventive policies will be based upon a uniform pattern of protein-calorie malnutrition and its age of onset. A qualitative classification is needed to distinguish patterns of severe malnutrition in hospitalized children, whereas a quantitative classification is a prerequisite in community studies of prevalence and severity. For community studies, classification should be based upon the indices of weight as percentage of expected weight at the given height calculated from the fiftieth percentile of the Boston standard, with limits proposed for the mild, moderate, and severe categories, and height as percentage of expected height for age, based upon the same standard. The Wellcome classification, which classifies malnourished children according to only the presence or absence of edema and a body weight above or below 60% of the Boston standard weight for age, has been proposed for qualitative classification of severe forms. (21 refs.) - *B. J. Grylack.*

London School of Hygiene and Tropical Medicine
London W.C.1, England

2203 ***CARNEY, M. W. P.; WEINBREN, I.; PURNELL, G. V.; & SHEFFIELD, B. F.** Reversal of adult mental subnormality. *British Medical Journal*, 3(5833):178, 1972. (Letter)

Mental subnormality was reversed in the case of a 27-year-old male presenting with the condition from birth and episodic confusion with behavioral disturbance. At laparotomy several islet-cell tumors in the head and tail of the pancreas were excised, and the diagnosis of multiple adenomatosis was confirmed histologically. It was impossible to remove all of the adenomata. The operation was followed by an absence of hypoglycemic symptoms and improvement in behavior, responsiveness, and intelligence, although the patient remains hyperparathyroid. The coincidence of improvement in symptoma-

tology and objective tests of intelligence with the institution of specific therapy and the rise in blood sugar in this case support the conclusion that restoration of the blood sugar to normal with diazoxide is the cause of the improvement. (4 refs.) - *B. J. Grylack.*

St. Annes-on-Sea
Lancs, England

2204 MCDONALD, K. M. Responsiveness of bone to parathyroid extract in siblings with pseudohypoparathyroidism. *Metabolism*, 21(6):521-531, 1972.

Urinary hydroxyproline excretion was used as an index of bone responsiveness, in an attempt for better specificity of response to parathyroid hormone in 4 cases of pseudohypoparathyroidism (PHPT) treated with parathyroid extract (PTE). The patients with PHPT (4 siblings) were compared with a group of 5 normal subjects and with a patient with primary hypoparathyroidism (HPT). During the first 4-8 days, all subjects were placed on a constant diet (90mg calcium, 500mg phosphorus, and less than 10mg hydroxyproline, daily) and 24-hr urine samples and blood samples were collected. For 4 subsequent days, PTE at 200 U every 6 hr was given; a final day of the study consisted of a continuation of the diet without the PTE and with continued sampling of urine and blood. Serum and urine calcium, inorganic phosphates, magnesium, and urinary hydroxyproline were determined, the latter by the method of Prockop and Udenfriend. All patients with PHPT showed impaired responses to PTE in calcium and inorganic phosphate excretion and a transitory increase in hydroxyproline, in contrast to the normal subjects and the patient with HPT, who maintained a high level of hydroxyproline until the injections were stopped. Correction of hypocalcemia by supplementary vitamin D did not restore sensitivity to PTE. The presence of separate genetic control of the adenyl cyclase enzyme in different tissues is possible, although bone and kidney were impaired in the cases studied here. (21 refs.) - *A. C. Schenker.*

University of Saskatchewan
Saskatoon, Canada

2205 ALVAREZ, LIA C.; DIMAS, CARMEN OLIVIA; CASTRO, ALBERTO; ROSSMAN, LAWRENCE G.; VANDERLAAN, EILEEN F.; & *VANDERLAAN, W. P. Growth hormone in malnutrition. *Journal of Clinical Endocrinology and Metabolism*, 34(2):400-409, 1972.

The effects of malnutrition on plasma growth hormone (hGH) and results of glucose loading in malnourished subjects were studied. The malnourished patients comprised 21 males and 15 females, hospitalized in San Salvador, Central America; normal controls were volunteers from women's jails. Glucose and insulin tolerance tests were conducted on all subjects, as well as the ratio of nonessential to essential amino acids and the growth hormone. Glucose was measured by the Nelson technique, amino acid ratio according to Whitehead, and the hGH by radioimmunoassay with the charcoal-dextran modification of Herbert. Malnourished patients showed mild glucose intolerance when compared to controls; after prolonged hospitalization (with better nutrition) the stimulatory effect of glucose administration was reflected in a slight attenuating effect on hGH secretion. Highly significant differences ($p<0.001$) were found in the plasma hGH concentrations both before and after glucose administration; glucose administration to malnourished women resulted in a rise in hGH concentration 2 hours later, and to malnourished men in a rise 1 hour later. A significant difference ($p<0.05$) was obtained in nonessential to essential amino acid ratio, 2.73:1 between women patients and controls, but not in men patients. It is suggested that hGH secretion is increased when the need for conservation of protein precursors is great. The limitations of short-term observations on fasting or protein deprivation are pointed out. (25 refs.) - *A. C. Schenker.*

Scripps Clinic and Research Foundation
La Jolla, California 92037

2206 DELANGE, FRANCOIS; ERMANS, ANDRE M.; VIS, HENRI L.; & STANBURY, JOHN B. Endemic cretinism in Idjwi Island (Kivu Lake, Republic of the Congo). *Journal of Clinical Endocrinology and Metabolism*, 34(6):1059-1066, 1972.

Syndromes associated with endemic cretinism, found in the northern half of Idjwi Island but

not in the southwest of the island, are described and their possible origin is discussed. Two overlapping syndromes are defined: one characterized by abnormalities in hearing and speech and neuromuscular disorders but with no thyroid function impairment, and the other by severe hypothyroidism. Results of a medical survey revealed an incidence of 5.3% of goiter in the southwest and of 54.4% in the north of the island. Of 99 cases of cretinism in the north, 10% were clinically euthyroid, all being deaf-mutes and 7 with a spastic diplegia of the lower limbs. The other 90% were characterized by growth and MR, marked lumbar lordosis with prominent abdomen, thickening of skin, delay in sexual development, and prolonged relaxation time of tendon reflexes. Thyroid scanning revealed the thyroid to be in its normal position. The thyroid stimulating hormone (TSH) value was extremely high in the blood, evidence for primary hypothyroidism and adequate pituitary function. The X-ray findings suggested that this type of cretinism could result from early fetal damage or damage in early infancy. (38 refs.) - *A. C. Schenker.*

Service des Radioisotopes
Hopital Saint-Pierre
1000 – Bruxelles, Belgium

2207 ELSAS, LOUIS J.; PASK, BEATRICE A.; WHEELER, FRANCES B.; PERL, DANIEL P.; & TRUSLER, SUZANNE. Classical maple syrup urine disease: cofactor resistance. *Metabolism*, 21(10):929-944, 1972.

An infant female who died from maple syrup urine disease (MSUD) on her thirteenth day of life failed to respond to cofactor stimulation. Diagnosis was based on the neonatal onset of progressive neurologic impairment, elevated plasma and urinary concentrations of the branched-chain amino acids and their alpha-keto acid derivatives, and an unremitting clinical course. Her cultured skin fibroblasts had less than 1% of normal decarboxylase activity for all 3 branched-chain amino acids, but decarboxylated pyruvate normally. Coenzymes stimulated cellular decarboxylation of pyruvate but not of branched chain amino acids. Cultured fibroblasts from her parents provided direct genetic evidence for an autosomal recessive mode of inheritance. In spite of appropriate therapy, instituted by the patient's eighth day of life, with resultant decreases in branched-chain amino acid and alpha-keto acid excretion, coma and apnea continued, and death ensued. The inhibitory effects of high concentrations of alpha-ketoisocaproic acid on decarboxylation of pyruvic acid, on protein synthesis, and amino acid transport by neural tissue presumably produced her central nervous system depression and downhill course. The mutant gene product in this patient appeared to be located on an apoenzyme containing a subunit common to all 3 branched-chain amino acid decarboxylases, which was not responsive to cofactor stimulation. (35 refs.) - *A. C. Schenker.*

Emory University School of Medicine
Atlanta, Georgia

2208 FRIEDMAN, PAUL A.; KAUFMAN, SEYMOUR; & KANG, ELLEN SONG. Nature of the molecular defect in phenylketonuria and hyperphenylalaninaemia. *Nature*, 240(5377):157-159, 1972.

Liver biopsy samples from an atypical phenylketonuria (PKU) patient and from 2 classical PKU patients were studied for hydroxylase activity. The atypical PKU liver was found to have 5-7% of the normal hydroxylase activity, whereas no detectable hydroxylase activity was found in the classical PKU samples. Immunological and kinetic properties of the hydroxylase in the hyperphenylalaninemic liver suggest that the enzyme in this patient is structurally distinct from the hydroxylase present in normal human liver. In the classical PKU liver samples, devoid of hydroxylase activity, no cross-reacting protein could be detected. Cross-reactivity of the antiserum with the atypical PKU extract was demonstrable if the extract was preincubated with antiserum. After 3 hr at 2°C no precipitate formed but the activity of the enzyme was inhibited; the data eliminated the possibility that a mutant, but antigenically identical, phenylalanine is present in atypical PKU liver at greater than 10% of the concentration in normal liver. The effects of L-phenylalanine concentration and of lysolecithin on the rate of tyrosine formation catalyzed by normal and atypical PKU livers led to the conclusion that the phenylalanine hydroxylase in the atypical PKU liver is a structurally altered enzyme compared with hydroxy-

lase from normal liver. (12 refs.) - *A. C. Schenker.*

National Institute of Mental Health
Bethesda, Maryland 20014

2209 **BALAZS, R.; & COTTERRELL, MARY.** Effect of hormonal state on cell number and functional maturation of the brain. *Nature*, 236(5346):348-350, 1972.

The effects of cortisol on postnatal cell formation in the rat brain were studied in an attempt to differentiate between behavioral effects produced by corticosteroids and thyroid hormone. In the cerebrum of the newborn, the cell number assessed by DNA determinations was 55% and in the cerebellum 3% of the adult value, which was reached at about 3 weeks after birth. Cortisol treatment led to a marked reduction in the normal increase in cell number. There was 90% inhibition in the cerebrum and 70% in the cerebellum between days 2 and 5, but after treatment was stopped the rate of increase in cell number was similar to that in the controls. To determine whether cortisol primarily affected cell formation or cell destruction, the synthesis of ^{14}C-DNA was studied 1 hr after the animals received an injection of 2-^{14}C-thymidine. During cortisol treatment, the formation of ^{14}C-DNA was strongly inhibited. There was a tendency to compensate for the initial cell deficit by accelerated mitotic activity in the treated animals, which ceased at the same age as in controls. Treatment with thyroid hormone advances the functional maturation of the brain, as indicated by the appearance of organized behavior, but these animals experience impaired adaptive behavior when they grow up. The different behavioral effects produced by corticosteroids and thyroid hormone may depend on their affecting different parts of the brain. (19 refs.) - *A. C. Schenker.*

MRC Neuropsychiatry Unit
Carshalton, Surrey, England

2210 **SHARMA, RAJ K.; *COLLIPP, PLATON J.; THOMAS, JOSEPH T.; & MADDAIAH, VADDANAHALLY T.** Abnormal glucose metabolism in diastrophic dwarfism. *Journal of the American Medical Association*, 222(9):1175-1177, 1972.

Although no biochemical abnormality has been previously reported in patients with features of diastrophic dwarfism, a 69 yr old patient showed abnormal glucose tolerance values, a high cholesterol level, very low growth hormone levels, and an abnormal response to tryptophan loading. He was observed to have short and deformed extremities, club feet, simian lines on both hands, strawberry nevus on the forehead, an incomplete cleft palate, and a pigeon-shaped chest with a protruding sternum. Mental development was normal. (This condition is not associated with MR and should be carefully distinguished from achondroplasia.) Serum cholesterol value was 184mg/100ml; triglycerides, 68mg/100ml. The fasting growth hormone assay showed values in nanograms/ml: less than 1.0, less than 1.0, 9.1, 2.4, less than 1.0, and 2.0 at 0, 20, 40, 70, 100, and 130 min, respectively. The metyrapone test showed 0.99 and 8.6mg 17-ketogenic steroid excretion for 24-hr urine speciments before and after administration of drug. Glucose tolerance test (with 2.0gm/kg body weight) showed 90, 210, 240, 208, and 140mg/ml glucose at 0, 30, 60, 120, and 180 min, respectively. Urinary excretion before and after L-tryptophan (100mg/kg) was 0.6 and 3.2mg xanthurenic acid and 1.0 and 12.0mg kynurenic acid. X-rays revealed scoliosis and lordosis of the spine, dysplastic hips, and flexion contractures of knee joints. (8 refs.) - *A. C. Schenker.*

*Nassau County Medical Center
East Meadow, New York 11554

2211 **WAISMAN, H. A.; SMITH, BARBARA A.; BROWN, ELEANOR S.; & *GERRITSEN, THEO.** Treatment of branched chain ketoaciduria (BCKA) during acute illness. *Clinical Pediatrics*, 11(6):360-363, June 1972.

A series of 11 acute episodes of metabolic acidosis in a girl with branched-chain ketoaciduria were successfully treated over a 6-yr period by the administration of bicarbonate in combination with the early restoration of metabolic equilibrium by intragastric feeding of a low branched-chain amino acid formula. At age 6 yrs, the girl is physically and mentally normal. The successful

outcome of this conservative procedure for correcting recurrent acidosis suggests that it should be considered by other physicians as a possible alternative to the more risky but commonly accepted treatment, peritoneal dialysis. Additionally, these findings may be applicable to the treatment of other inborn errors of metabolism, such as ketotic hyperglycinemia and methylmalonic aciduria, where infection is an ever-present problem. (9 refs.) - *N. Mize.*

*University of Wisconsin Medical Center
Madison, Wisconsin 53706

2212 **BROWN, ROY E.** Some nutritional considerations in times of major catastrophe. *Clinical Pediatrics*, 11(6):334-342, 1972.

Recent experience in India's Bangladesh refugee camps only reemphasizes the need to develop suitable emergency programs for coping with such catastrophic situations of widespread malnutrition and ill health in children. In addition to taking care of the obvious problems, such as feeding, correction of anemia, treatment of parasites, malaria, infectious diseases, and skin conditions, physicians and trained personnel should be alerted to the desirability of encouraging lactation, both psychologically and medically, in mothers with young children. This uncontaminated, cheap source of nutrition provides badly needed protein and eliminates the problems of formula preparation among an illiterate population. Also, depending on the facilities and funds available, adequately supervised training programs for health personnel, as well as a system of record-keeping and periodic evaluation, need to be established as a way of ensuring that health advances will not be merely short-term. (24 refs.) - *N. Mize.*

Mount Sinai School of Medicine
New York, NY 10029

2213 **LEVY, HARVEY L.; MADIGAN, PHYLLIS M.; & SHIH, VIVIAN E.** Massachusetts Metabolic Disorders Screening Program. I. Technics and results of urine screening. *Pediatrics*, 49(6):825-836, 1972.

Urine screening of 222,302 infants during the past 3 years as part of the Massachusetts Metabolic Disorders Screening Program has resulted in the detection of a metabolic disorder in 64 infants. Cystinuria has been most common, with similar frequencies found for histidinemia, Hartnup disease, and iminoglycinuria. Each of these 4 disorders has a frequency comparable to that of phenylketonuria in Massachusetts (1:14,219). Among the transient disorders noted were tyrosinuria-tyrosyluria, generalized hyperaminoaciduria, iminoglycinuria, cystine-lysinuria, hyperglycinuria, and hyperlysinuria. As a result of this program, infants with metabolic disorders for which treatment is desirable have been diagnosed and begun on treatment early in life. Almost 80,000 infants are screened yearly in this program, at least 1 urine specimen from each infant being tested by 3 separate chromatographic procedures and an additional test being performed on 8.1% of all specimens. This urine screening program may be the most comprehensive in existence for the detection of metabolic and renal transport defects. Such a program is complicated and requires a great deal of cooperation among participating groups. The total cost of the program is approximately $80,000 yearly or $1.00 per infant tested. (37 refs.) - *B. J. Grylack.*

State Laboratory Institute
Boston, Massachusetts 02130

2214 **BUCHSBAUM, MONTE; KING, CATHY; & HENKIN, ROBERT I.** Average evoked responses and psychophysical performance in patients with pseudohypoparathyroidism. *Journal of Neurology, Neurosurgery, and Psychiatry*, 35(2):270-276, 1972.

Eight patients (aged 13-48yr) had pseudohypoparathyroidism (PHP) in which kidney and bone are resistant to parathyroid hormone. The features of PHP include brachydactyly, round facies, short stature, obesity, MR (IQ below 90 in 5 or 8), hyposmia, elevated taste thresholds for sour and bitter, abnormal EEG, and hypocalcemia. Average evoked response (AER) results included significantly longer latency among PHP than among 80 (aged 18-31) normal controls, and less decrease in latency with increasing light intensity. Increased latency was associated with elevated serum calcium (above 9mg/100mg), as mean latencies at N_{120} were 174msec and 142msec for PHP with high and low calcium respectively. Low IQ was associated with long AER latency. Nerve

conduction velocity varied widely among PHP (47 to 76m/sec) with a mean of 62m/sec vs. a mean of 56m/sec for normals. Cerebral calcifications were associated with a negative AER slope. Psychophysical test results included abnormal performance by 7 of 8 in the rod and frame test, overestimation of disk size, and slower reaction times. The Set Index of the patients was significantly different from that of the normal volunteers. The investigation of neurophysiological or perceptual deficits can offer not only diagnostic clues about the disease, but insights into perceptual processes. (30 refs.) - *V. J. Goldberg.*

National Institute of Mental Health
Bethesda, Maryland

2215 **JOHNSON, CHARLES F.** Phenylketonuria and the obstetrician. *Obstetrics and Gynecology*, 39(6):942-947, 1972.

Pregnant women with elevated blood phenylalanine levels risk giving birth to microcephalic, small-for-dates babies with multiple congenital abnormalities and future MR. In maternal-type hyperphenylalaninemia, fetal damage occurs *in utero* and the child may well have normal phenylalanine levels after birth. Elevated amino acid levels occur after birth in classic hyperphenylalaninemia because the excess amino acid of the fetus is metabolized by its mother. In classic phenylketonuria, the infant is homozygous for the disease and will show elevated blood phenylalanine levels which may be treated by diet. In cases of maternal hyperphenylalaninemia, characterized by amino acid levels above 20mg%, it is recommended that pregnancy be avoided or terminated. The efficacy of low phenylalanine diets during pregnancy for women with slightly elevated phenylalanine levels (10 to 14mg%) is not known. Screening for hyperphenylalaninemia is recommended for women showing a family or personal history of phenylketonuria, MR, microcephaly, abortion, infertility, intrauterine growth retardation, or transient neonatal hyperphenylalaninemia. Premarital screening of all women should also be considered. (14 refs.) - *V. J. Goldberg.*

University of Iowa School of Medicine
Iowa City, Iowa 52240

2216 **BUXTON, P.; CUMINGS, J. N.; ELLIS, R. B.; LAKE, B. D.; MAIR, W. G. P.; ROBERTS, J. R.; & YOUNG, E. P.** A case of G_{M2} gangliosidosis of late onset. *Journal of Neurology, Neurosurgery, and Psychiatry*, 35(5):685-692, 1972.

Clinical findings in a 10-yr-old boy with late-onset G_{M2} gangliosidosis included normal development to age 5, uncontrollable tonic seizures, loss of fine muscle control, and abnormal EEG. Later he had frequent prolonged tonic-clonic fits, dementia, MR, spontaneous tremors in the arms, but no sensory loss. Histological findings in brain biopsy material included distension of the cortical neuronal and glial cells due to finely granular cytoplasmic material compressing nuclei to cell edges. Electron microscopy revealed membranous bodies formed by parallel or concentric arrays of laminae, electron lucent nuclei, scant mitochondria, and other typical Tay-Sachs findings. There were no significant abnormalities in the amount or proportions of phospholipid or sphingolipid. The hexosaminidase A (heat labile) activity in grey matter and leukocytes was typical of Tay-Sachs' disease, and the DEAE chromatography of brain supernatant gave a hexosaminidase elution profile also similar to that found in Tay-Sachs. In other cases of late-onset hexosaminidase A deficiency, the enzyme activity was intermediate between normal and Tay-Sachs levels. A healthy younger sister had the same levels of hexosaminidase A as the patient, indicating that the defect was present from an early age; however, it is unclear why some children can lead several years of normal life while others may be affected in their first year of life. (14 refs.) - *V. J. Goldberg.*

Walton Hospital
Liverpool, England

2217 **STEIN, ZENA; SUSSER, MERVYN; SAENGER, GERHART; & MAROLLA, FRANCIS.** Nutrition and mental performance: Prenatal exposure to the Dutch famine of 1944-1945 seems not related to mental performance at age 19. *Science*, 178(4062):708-713, 1972.

A retrospective study investigated the relationship between prenatal exposure to food deprivation and the subsequent development of intelligence in the 19-year-old male offspring. The study population comprised 125,000 military

inductees born in either cities affected by famine conditions or in control cities during the 3-year period from January 1, 1944, to December 31, 1946; 20,000 of these were inferred to be exposed to the famine through maternal starvation. Overall, the frequency of MR (severe or mild) among survivors of the birth cohorts was not related to conception or birth during the famine years. The later postwar rise in the frequency of mild MR can be accounted for by the rebound in fertility of the lower classes after the famine. The results point either to a high order of protection afforded the fetus *in utero* or to great resilience of the fetus in the face of nutritional insult, or to both. The results affirm the association of social environment and mental performance. (20 refs.) - *A. C. Schenker.*

Columbia University School of Public Health and Administrative Medicine
New York, New York 10032

2218 **HUTTENLOCHER, PETER R.; & AMEMIYA, IKUKO M.** Effects of adrenocortical steroids and ACTH on Na+-K+ ATPase and on Na+ and K+ concentrations in immature cerebral cortex. *Neurology*, 22(4):428, 1972. (Abstract)

Mechanisms of adrenocortical hormones and ACTH anticonvulsant action were studied in infant and weanling rats and young kittens. Ss were treated for 3 days with hydrocortisone (0.02 mg/gm/day), methylprednisolone (0.01mg/gm/day), or ACTH gel (0.015 units/gm/day). Na+-K+ ATPase was determined in whole brain homogenates and in microsomal fractions at pH 7.6. Enzyme activity in hormone-treated groups was 15-30% above that in controls. In weanling rats treated with methylprednisolone, this activity, in the light microsomal fraction, was 7.07 micro-M.P'/mg protein/10 min versus 5.46 in controls ($p<0.01$). Brain potassium concentration was higher in methylprednisolone-treated infant rats (89mEq/kg wet brain) than in controls (84.1mEq/kg wet brain) ($p<0.05$). The difference was more marked in animals receiving repeated electroshock. Total brain protein increased slightly from 75.1mg controls to 77.4mg in steroid treated rats, and protein concentration increased markedly from 123.9 to 148.4mg/gm brain. The results suggest a functionally stimulating effect of adrenocortical steroids on the sodium pump system in developing brain. - *A. C. Schenker.*

2219 **PEARL, MARILYN; FINKELSTEIN, JACK; & BERMAN, MICHAEL.** Temporary widening of cranial sutures during recovery from failure to thrive. *Clinical Pediatrics*, 11(7):427-430, 1972.

A temporary separation of cranial sutures was found to be associated with the initiation of therapy for severe malnutrition and failure to thrive in 2 young Puerto Rican children, aged 18 mos and 5 mos. Serial roentgenograms showed a gradual return to normal over a period of several weeks. Lumbar puncture showed a normal CSF in both children and the recovery from failure-to-thrive was satisfactory in both cases. This syndrome is most common among nutritionally deprived infants with a head size below the third percentile at the start of treatment. The relatively faster growth in brain size as compared to size of the cranial vault is most likely responsible. (14 refs.) - *N. Mize.*

Metropolitan Hospital
New York, NY 10029

2220 **ZIAI, MOHSEN; & *DEELY, NICHOLAS.** Progressive neurologic disease and blindness in an infant. *Clinical Pediatrics*, 11(2):125-126, 1972.

An emaciated 1-yr-old boy with a history of mental and physical deterioration was referred for clinical examination. The child was the product of an unremarkable pregnancy and had appeared to develop normally during the first few months of life, when sudden regression set in. A degenerative disorder of the central nervous system was suspected. The major clinical finding, apparent blindness associated with a "cherry red spot" at the macula, provided the key to a Tay-Sachs disease diagnosis, a diagnosis which was supported also by strong evidence of Jewish ancestry. - *N. Mize.*

*Fairbanks Medical and Surgical Clinic
Fairbanks, Alaska

2221 **MCKUSICK, VICTOR A.; HOWELL, R. RODNEY; HUSSELS, IRENE E.;**

NEUFELD, ELIZABETH F.; & STEVENSON, ROGER E. Allelism, non-allelism, and genetic compounds among the mucopolysaccharidoses. *Lancet*, 1(7758):993-996, 1972.

Cellular examination of 5 cases of inherited mucopolysaccharidoses difficult to categorize suggests that the genes for the strikingly dissimilar Hurler and Scheie syndromes are allelic. In 4 of the cases studied, the clinical characteristics and the correctibility of fibroblasts suggest genetic compounds of the MPS.1 (Hurlers syndrome)/MPS.V (Scheie syndrome) type. The result is an intermediate phenotype with features distinctly different from any of the established categories. In the fifth case, the 31-year-old patient's fibroblasts showed a functional deficiency of the same protein characteristically lacking in the Maroteaux-Lamy syndrome, but his phenotype most closely resembled the Scheie syndrome. Pending further investigation, the patient's disorder, possibly due to homozygosity of an allele at the MPS VI locus, is referred to as MPS VI-B. (32 refs.) - *N. Mize.*

Johns Hopkins Hospital
Baltimore, Md. 21205

2222 GRANT, E. H.; SHEPPARD, R. J.; MILLS, G. L.; & SLACK, JOAN. A dielectric investigation of the water of hydration of low-density lipoproteins in familial hyperbetalipoproteinemia. *Lancet*, 1(7761):1159-1161, 1972.

The dielectric constant of low-density lipoproteins (LDL) in the sera of two heterozygotes and one homozygote with familial hyperbetalipoproteinemia has been found to be significantly lower ($p<0.001$) than the mean values for 3 normal controls. The difference is probably best expressed as an increase in the water of hydration (W) associated with the LDL in familial hyperbetalipoproteinemia. Using a simple molecular model, the mean value of W in the normal Ss was 0.03, in the heterozygotes, 0.09, and in the homozygote, 0.14. Even though the number of Ss involved in this study is small, these findings, coupled with those of other investigators, support the contention of significant differences at the molecular level between normal serum LDL and that produced by the gene responsible for the described types of familial hyperbetalipoproteinemia. (16 refs.) - *N. Mize.*

Queen Elizabeth College
London W8 7AH, England

2223 EBRAHIM, G. J. Vitamin A deficiency—a continuing health problem in developing countries. *Clinical Pediatrics*, 11(11):610-612, 1972.

The problem of acute vitamin A deficiency, a major cause of blindness among children in the underdeveloped countries, indicates clearly the need for widespread programs of health and nutrition education. Because of the common etiologic factors, vitamin A deficiency often occurs in association with protein-calorie malnutrition. When untreated, the disease progresses rapidly to keratomalacia and then to total destruction of the cornea. Some experimental community approaches to the problem, including a preschool protection program and a nutrition rehabilitation center, have proven successful but need to be expanded. In the meantime, a relatively inexpensive program providing massive doses of vitamin A once a year to preschool children has markedly reduced xerophthalmia in an experimental group of Indian children and should be considered a useful interim measure elsewhere. (12 refs.) - *N. Mize.*

Hospital for Sick Children
London, England

2224 JOHNSON, CHARLES F. What is the best age to discontinue the low phenylalanine diet in phenylketonuria? *Clinical Pediatrics*, 11(3):148-156, 1972.

A group of 17 clinical centers are participating in a national collaborative study aimed at resolving current scientific controversy as to the best age for discontinuing the low phenylalanine diet in children with phenylketonuria. The success of this study is jeopardized, however, by the already announced intentions of the participants to continue the diet in phenylketonuric Ss, in any case, beyond 6 years—thereby hampering the group's ability to collect adequate discontinuation data. To date, the major followup studies in this area have focused on 2 groups of phenylketonuric

children: those in whom the low phenylalanine diet was initiated by the age of 11 mos. ("early starters") and those started at a later time when the prospects for controlling the associated MR were greatly lessened. In both of these groups, the special diet was discontinued at some time between the age of 6 and 9 yrs. No significant decrease in intellectual performance or behavior was observed in either group, though the small sample size makes it impossible to draw any definite conclusions. Further well-designed follow-up studies through the school years would make an important contribution to this question. (11 refs.) - *N. Mize.*

University of Iowa
Iowa City, Iowa 52240

2225 X linkage of human galactosidase. *Nature*, 240(5375):14, 1972.

Use of the interspecific somatic cell hybridization technique has shown that human galactosidase is probably X-linked. When Chinese hamster cells deficient in thymidine kinase were fused with human diploid fibroblasts lacking hypoxanthine-guanine phosphoribosyl transferase, it was found that hybrid cells which retained human galactosidase also retained 3 X-linked markers and that loss of galactosidase correlated with loss of these markers. Use of the technique to investigate the linkage relationships of induced mutations of Chinese hamster cells indicated that at least 3 of the recessive mutations and their wild type alleles are not linked. - *B. J. Grylack.*

2226 **CASAZZA, LAWRENCE J.** Effect of protein supplementation on humoral immune response mechanism in growing children. *Lancet*, 2(7784):980-981, 1972. (Letter)

Valuable research in the area of nutrition-immunity interactions requires screening methods that can select anthropometrically and/or biochemically those who would be poor risks for a vaccination. Additionally, it requires adequate long-term follow-up for titer levels and history of possible loss of clinical protection. Any less effective vaccine program might further harm the marginal nutritional status of the target population. - *B. J. Grylack.*

Tulane University
New Orleans, Louisiana 70112

2227 **CRAWHALL, JOHN C.; & BANFALVI, MARIANNE.** Fabry's disease: differentiation between two forms of α-galactosidase by myoinositol. *Science*, 177(4048):527-528, 1972.

Results of a study of the effect of the inhibitor myoinositol on α-galactosidase activity in 3 patients with Fabry's disease and in normal control cells support the hypothesis, proposed on the basis of Michaelis constant (K_m) data and electrophoretic separation of 2 different enzymes from leukocytes, that there is a separate heat-labile enzyme that is absent in the X-linked condition Fabry's disease. The data demonstrated that the residual α-galactosidase enzyme found in fibroblast cells of the Fabry's disease patients was characterized by its higher K_m, its resistance to heat inactivation, and the lack of inhibition by myoinositol. Myoinositol had no inhibitory effect on the β-galactosidase activity in fibroblasts. (6 refs.) - *B. J. Grylack.*

Royal Victoria Hospital
Montreal, Quebec, Canada

2228 **METCOFF, JACK; WILKMAN-COFFELT, JOAN; YOSHIDA, TAKASHI; BERNAL, ALFONSO; ROSADO, ADOLFO; YOSHIDA, PABLO; URRUSTI, JUAN; FRENK, SILVESTRE; MADRAZO, RICARDO; VELASCO, LUIS; & MORALES, MYRIAM.** Energy metabolism and protein synthesis in human leukocytes during pregnancy and in placenta related to fetal growth. *Pediatrics*, 51(5):866-877, 1973.

Studies which indicate some patterns of energy metabolism and protein synthesis during the last trimester of pregnancy are reported; these studies were prompted by an attempt to discover the characteristics of malnutrition in fetuses *in utero*. Metabolism of the peripheral blood leukocyte was considered to be a good index of cell metabolism in organs such as the liver and muscle, especially since enzyme defects could also be found in the leukocyte. Consequently, maternal leukocyte metabolism was observed; energy metabolism, revealed by the adenosine triphosphate (ATP) levels and adenylate and pyruvic kinase activities; RNA synthesis, investigated by RNA polymerase activity. These activities were found to increase in normal mothers during the last 6-8 weeks of gestation, and RNA

synthesis appeared to correlate with the birthweight of the infant. The low levels, previously reported in women having fetally malnourished babies, indicate some defect in energy metabolism. (47 refs.) - *A. C. Schenker.*

Children's Memorial Hospital
Oklahoma City, Oklahoma 73190

2229 **MUNRO, HAMISH N.** Leukocytes and fetal malnutrition. *Pediatrics*, 51(5):926-928, 1973.

Metcoff's work, relating changes in the energy metabolism of leukocytes to the degree of postnatal malnutrition of young children, is reviewed. In recent published work, Metcoff's group described measurements of fetal leukocytes, maternal leukocytes, and the placenta, which indicate their capacity to generate energy and in some instances to synthesize RNA and protein. In the infants with intrauterine malnutrition (IUM) the fetal leukocytes were larger than in premature infants without growth failure (AGA) or in full term infants (FT). These leukocytes, however, had a low adenosine triphosphate (ATP) content per cell as well as a low pyruvate kinase and adenylate kinase. It emerged from measurements of maternal leukocytes that, while enlarged maternal leukocytes with low energy capacity are characteristic of IUM, low RNA polymerase levels in maternal leukocytes are associated with low birthweight from all causes. Fetal growth retardation affects about 3% of births in developed countries and up to 10% in developing countries, where malnutrition may be a major contributing factor. A potential predictive test may be developed in the form of changes in maternal leukocyte size and energy metabolites. (9 refs.) - *A. C. Schenker.*

Massachusetts Institute of Technology
Cambridge, Massachusetts

2230 **SCHAIN, RICHARD J.; WATANABE, KATHY; & HAREL, SHAUL.** Effects of brief postnatal fasting upon brain development of rabbits. *Pediatrics*, 51(2):240-250, 1973.

The effects of total fast during the first 2 days of postnatal life upon subsequent brain development were studied in 34 developing (17 pairs from 7 does) New Zealand white rabbits. The pairs were divided into 2 groups, experimental and control; both groups were maintained in an incubator at 35°C during the first 3 days of life. The controls were placed in the doe's cage every morning for 10-15 min, whereas the experimental group missed 2 morning feedings. When the fasted animals were similarly returned to the does, some were observed to catch up in body growth promptly after termination of fasting (group I); others remained below the control animals' weight (about 25% or greater) and were treated as a separate group (group II). The brain and body weights of the fasted animals of group II were significantly below the control animals; there were no such differences in the group I animals compared with their controls. All cerebral constituents in the group II animals were significantly below control animals; cholesterol was reduced to a greater extent than DNA, RNA, and protein. No significant differences were seen in group I and controls. It is suggested that intensive early postnatal feeding may prevent brain damage in human low birthweight infants. (27 refs.) - *A. C. Schenker.*

UCLA School of Medicine
Los Angeles, California 90024

2231 **DANKS, D. M.; CAMPBELL, P. E.; WALKER-SMITH, J.; STEVENS, B. J.; GILLESPIE, J. M.; & BLOMFIELD, J.** Menkes' kinky-hair syndrome. *Lancet*, 1(7760):1100-1102, 1972.

Studies of copper status in 7 babies with the typical clinical features of Menkes' kinky hair syndrome—progressive mental deterioration, disturbance of muscle tone, variable hypothermia, pili torti, and characteristic facies—have demonstrated a common copper deficiency in all. Serum copper and copper oxidase levels were typically lower than those found even in nutritional copper deficiency, yet nutrition was not a factor. Overall, the observed deficiency is consistent with gross changes in the free sulphydryl groups in hair keratin, which would explain the kinky hair, and is probably also responsible for changes in the arterial wall fibers, scorbutic bone changes, and hypothermia. Defective intestinal absorption of copper is the most likely explanation. Further research should delineate the precise disturbance, thereby making treatment of this disorder a possibility. (26 refs.) - *N. Mize.*

Royal Childrens Hospital Research Foundation
Victoria, Australia

2232 **WALDMANN, THOMAS A.; & MCINTIRE, K. ROBERT.** Serum-alpha-fetoprotein levels in patients with ataxia-telangiectasia. *Lancet*, 2(7787):1112-1115, 1972.

Measurement of the serum-α-fetoprotein concentrations of 20 patients with ataxia/telangiectasia, 149 normal children and adults, 15 siblings and 11 parents of patients with ataxia/telangiectasia, and 54 patients with other immunodeficiency states revealed raised α-fetoprotein levels (above 30ng/ml) in each of the 20 patients with ataxia/telangiectasia but not in any other group. The synthesis of the fetal protein of hepatic origin, α-fetoprotein, by patients with this disorder suggested that at least 1 nonlymphoid organ, the liver, is not fully developed in these individuals. The findings supported the hypothesis that a primary abnormality of these patients is a defect in tissue differentiation, perhaps due to a defective interaction between the entodermal and mesodermal germ lines, necessary for normal differentiation of digestion associated organs. (21 refs.) - *B. J. Grylack.*

National Cancer Institute
Bethesda, Maryland

2233 **GOLDHAMMER, Y.; BUBIS, J. J.; SAROVA-PINKAS, IDA; & BRAHAM, J.** Subacute spongiform encephalopathy and its relation to Jakob-Creutzfeldt disease: report on six cases. *Journal of Neurology, Neurosurgery, and Psychiatry*, 35(1):1-10, 1972.

Clinical, electroencephalographic, and pathologic findings in six cases of the subacute spongiform encephalopathic (SSE) form of Jakob-Creutzfeldt (J-C) disease indicate that the disorder has a recognizable pattern during life. Early signs of weakness, headache, and minor mental or emotional disturbances were followed in each case by signs of dementia, confusion, and speech difficulties progressing to akinetic mutism and myoclonus. All six patients died within three months of first appearance of symptoms. All EEG patterns in this series of cases show repetitive bisynchronous single mono- or biphasic sharp waves, with high voltage slow activity and without normal background rhythms. Histological changes in brain gray matter include loss of neurones, astrocytosis, and status spongiosus, the latter to a varying degree. (Traces of histological change may be so slight that only the combination of clinical and EEG findings can be considered diagnostic.) Some demonstrators have investigated the possibility that J-C is a slow virus disease by (successfully) attempting to transmit the SSE form among chimpanzees; others have noted virus-like particles in electron microscope study of affected brains. Ischemia has also been suggested as an etiologic factor. Idoxyuridine therapy was unsuccessful in the one case in which it was tried; in a later case outside this series, amantadine was used with some success. (36 refs.) - *N. Jarvis.*

Tel Aviv University Medical School
Tel Aviv, Israel

2234 **HUNTER, RICHARD; DAYAN, A. D.; & WILSON, JOHN.** Alzheimer's disease in one monozygotic twin. *Journal of Neurology, Neurosurgery, and Psychiatry*, 35(5):707-710, 1972.

A pair of monozygotic twins apparently discordant for Alzheimer's disease, the second such case reported in the literature, is described. One sister died at age 64 in a state of profound dementia from a disease that had begun about 15 years previously with personality change and paranoia, developing through amnesia to total social incapacity. Her brain proved to be atrophic, with marked wasting over frontal and occipital lobes. There were large numbers of argyrophilic plaques in the cortex, neurofibrillary tangles in cortical neurones, and a generalized neuronal loss. Her sister died at the age of 66 of malignant cachexia. Finger prints, blood group analysis, and biochemical markers of the twins confirmed that they were monozygous. Except for some recent memory impairment and a minor EEG abnormality (which could be attributed to other causes) there was no evidence that the second twin was affected with Alzheimer's disease. The fact that no case of twins with Alzheimer's disease has ever been reported, whereas this is the second pair of twins discor-

dant for the disease, suggests that exogenous factors may be important in etiology, familial Alzheimer-like cases perhaps constituting a separate disease entity. (14 refs.) - *N. Jarvis.*

Friern Hospital
London, England

2235 **ZORAB, PHILLIP; & EDWARDS, HAROLD.** Spinal deformity in neurofibromatosis. *Lancet*, 2(7781):823, 1972. (Letter)

Detailed examination of 5 patients (CA range 18 to 38 years) with very severe lateral curvature of the spine but without signs of cord pressure or stretching showed the nervous system to the trunk to be entirely normal. This finding suggested that spinal curvature in these cases was not caused by any primary abnormality of the nervous system. A bony or a muscle disorder may be responsible for the scoliosis. (6 refs.) - *B. J. Grylack.*

Institute of Diseases of the Chest
Brompton, London S.W.3, England

2236 **ISHINO, HIROSHI; MII, TAKASHI; HAYASHI, YASUAKI; SAITO, AKIRA; & OTSUKI, SABURO.** A case of Wilson's disease with enormous cavity formation of cerebral white matter. *Neurology*, 22(9):905-909, 1972.

A girl who died at age 12 had Wilson's disease with cavity formation in the white matter as well as changes in the pallium and cerebellum. The disintegration of the cerebral white matter and, to a lesser degree, the cerebral cortex provided a morphologic background for the clinical symptoms of mutism, frequent convulsive seizures, and myoclonic phenomena. There was remarkable sparing of the hippocampal formation, calcarine areas, and the anterior portions of cingulate convolution and gyri recti, regions that are oldest from the standpoint of myelogenesis and the most resistant to the pathologic process of Wilson's disease. The finding of vascular congestion in both the cerebrum and cerebellum, hemorrhagic foci of different ages, enlargement of perivascular spaces with connective tissue proliferations, parenchymal necroses of the occipital cortex, and detachment of molecular layer from granular layer together with homogenizing changes of the Purkinje cells suggested the presence of circulatory disturbances. (12 refs.) - *B. J. Grylack.*

Okayama University Medical School
Okayama, Japan

2237 **ROSZEL, J. F.; STEINBERG, S. A.; & MCGRATH, J. T.** Periodic acid-Schiff-positive cells in cerebrospinal fluid of dogs with globoid cell leukodystrophy. *Neurology*, 22(7):738-742, 1972.

Cytologic examination revealed large globoid cells with periodic acid-Schiff-positive granules in the cerebrospinal fluid and brain sections from 4 West Highland white terriers with clinical and morphological indications of globoid cell leukodystrophy but did not show any of these cells in the cerebrospinal fluid of 3 control dogs without a neurological disorder. The study showed that the use of membranes that retain virtually all the cells and examination of large volumes of fluid may be beneficial in demonstrating these cells in early clinical cases or even in preclinical cases when hereditary factors suggest this diagnosis. The use of membranes with appropriately larger pore sizes should make it possible to obtain nearly pure preparations of globoid cells for electron microscopic examination. (13 refs.) - *B. J. Grylack.*

College of Veterinary Medicine
Oklahoma State University
Stillwater, Oklahoma 74074

2238 **SIMOPOULOS, ARTEMIS P.; ROTH, JOEL A.; GOLDE, DAVID W.; & BARTTER, FREDERIC C.** Subacute necrotizing encephalomyelopathy with vacuolated cells in the bone marrow. *Neurology*, 22(12):1257-1267, 1972.

The association of subacute necrotizing encephalomyelopathy with respiratory alkalosis, hypokalemia, hypomagnesemia, aldosteronism, and vacuolation of bone marrow was reported for the first time. The vacuolation in the bone marrow and brain and spinal cord appeared to be thiamine dependent, and a new variant of subacute necrotizing encephalomyelopathy may have been represented in the patient, a female child. The proposita exhibited clinical and histologic changes consistent with Leigh's disease, although both appeared to be modified by thiamine supplementation, which

resulted in the elimination of an inhibitor of thiamine pyrophosphate-adenosine triphosphate phosphotransferase from the serum and urine and in the disappearance of the vacuoles from bone marrow cells. Spironolactone corrected the hypokalemia without additional CK1, and $MgCl_2$ corrected the hypomagnesemia. Autopsy revealed vacuolation of white matter and gray matter, dorsal columns of the spinal cord, and bone marrow, and myelin loss in the white matter and dorsal columns. (31 refs.) - *B. J. Grylack.*

2101 Constitution Avenue, N.W.
Washington, D. C.

2239 **GOLDSTEIN, MENEK; FREEDMAN, LEWIS S.; BOHUON, AGREGE C.; & GUERINOT, FRANCOISE.** Serum dopamine-β-hydroxylase activity in neuroblastoma. *New England Journal of Medicine*, 286(21):1123-1125, 1972.

Twelve of 22 (1 to 11 yr-old) neuroblastoma patients had serum dopamine-β-hydroxylase (DBH) activities in the range of 27 control children, and 10 had serum DBH levels 3 or more times higher than controls. Elevated DBH was associated with increased urinary vanillymandelic acid. In C-1300 mice with neuroblastoma the serum DBH activity was proportional to tumor size. The vascularization and the location of the tumor, and the age of the patient also affect catecholamine and DBH release. (16 refs.) - *V. J. Goldberg.*

New York University Medical Center
New York, N. Y. 10016

2240 **GROSSMAN, A. B.** Tapetoretinal degeneration. *British Medical Journal*, 1(5797):443, 1962. (Letter)

In contrast to the theory that the b-wave of the electroretinogram is due principally to electrical changes occurring in the bipolar cells of the retina, it has been proposed that the b-wave is almost exclusively due to depolarization of the glial (Muller) cells. This latter view, which has a considerable amount of circumstantial evidence to support it, has the merit of equating the b-wave with such gross retinal neuronal activity leading to a net increase in extracellular potassium, which is sufficient to depolarize the highly potassium-sensitive glia. (1 ref.) - *B. J. Grylack.*

University College
London W.C.1, England

2241 **KRAUS-RUPPERT, R.; WILDBOLZ, A.; MATTHIEU, J. M.; & HERSCHKOWITZ, N.** The late form of metachromatic leukodystrophy: 1. A histochemical and neurochemical study. *Journal of the Neurological Sciences*, 174(4):373-381, 1972.

A late form of metachromatic leukodystrophy (MLD) is reported in a 39-year-old man who had previously been asymptomatic; neuropathological and neurochemical data are described. A psychomotor syndrome with stammering and tremor dominated the clinical picture. With progression of the disease, hemiparesis and, shortly before death (at age 45), spasticity and a febrile peak were seen. Symmetrical demyelination with glial reactions and preserved U-fibres was prevalent; metachromatic sulphatide-containing deposits were observed in the white matter, in the glial nerves and nerve cells, and in macrophages. The results indicated that in the late form of MLD the deposited substances consist mainly of cerebroside sulphate esters with carbohydrate moieties and phospholipids. An overall reduction in the levels of all lipids was shown neurochemically. The pathological changes in the cortical and glial cells, in the endothelial cells of small blood vessels, and in the meningeal macrophages have not previously been described in the late form of MLD. (29 refs.) - *A. C. Schenker.*

University of Berne
Berne, Switzerland

2242 **KRAUS-RUPPERT, R.; & SOMMER, H.** The late form of metachromatic leukodystrophy: II. Ultrastructural correlations with morphological and neurochemical findings. *Journal of the Neurological Sciences*, 17(4):383-387, 1972.

Ultrastructural details of a case of a late form of metachromatic leukodystrophy are reported. These investigations confirm the histochemical and neurochemical results in a previous study of this case. Intracytoplasmatic osmiophilic deposits were observed in glial cells of the white matter, in

cortical nerve cells, and in the endothelial cells of the brain capillaries. The results of the ultrastructural investigations agree in general with the findings of other authors, especially with respect to the changes in glial cells and extraneuronal tissues in the infantile and juvenile stages. (11 refs.) - *A. C. Schenker.*

University of Berne
Berne, Switzerland

2243 **PILZ, H.; & HOPF, H. C.** A preclinical case of late adult metachromatic leukodystrophy? *Journal of Neurology, Neurosurgery, and Psychiatry*, 35(3):360-364, 1972.

Urine analyses of siblings of a patient with the late adult form of metachromatic leukodystrophy (ML) revealed a case of ML in a 39-year-old woman identified by deficiency of arylsulfatase A in urine and leukocytes, increased excretion of sulfatide in urine, and an accumulation of metachromatic substances in the epithelial cells of the urine sediment. Neurological examination revealed definite decrease of motor nerve conduction velocities in upper and lower extremities. There were no cerebral symptoms. Biochemical anomalies were so extensive as to rule out a latent form of ML, nor can the symptoms be interpreted as expressing a heterozygote hereditary tendency. The case is thought to be late adult ML, discovered before the first subjective disorders manifest themselves; further symptoms are expected to develop. (23 refs.) - *N. Jarvis.*

University of Gottingen
Gottingen, Western Germany

2244 **AUSTIN, JAMES H.** Studies in metachromatic leukodystrophy: XII. Multiple sulfatase deficiency. *Archives of Neurology*, 28(4):258-264, 1973.

Current information about the multiple sulfatase deficiency (MSD) form of metachromatic leukodystrophy (MLD) is summarized, and a case of MSD-MLD is reported. The patient was a 10-month-old boy who was hospitalized because of slow development. The child died at age 11 years, after progressive deterioration, with laboratory evidence of a marked increase in urinary sulfatides. Postmortem paraffin sections of the brain showed marked atrophy of gray matter of cerebrum and cerebellum. The basic findings throughout the central and peripheral nervous systems were those of late infantile MLD. Bone marrow cells from the patient and his sister were cultured in 3 different media and showed abnormal granules which persisted in neutrophils and normal eosinophil granules which tended to make their first appearance in tissue culture only. The family history supported the assumption of an autosomal recessive mode of inheritance. In the case reported, and in a previous report on a sister of this child, retinal atrophy exceeded that found in conventional MLD of a comparable age and evolution. Autopsy tissues showed multiple deficiencies of arylsulfatase A, B, and C. Findings in relevant cases in the literature include increase in glycolipids, in glycosaminoglycuronoglycan sulfates, and in A steroid sulfate. It is suggested that the same type of molecular error may be present in all 3 sulfatases. (32 refs.) - *A. C. Schenker.*

University of Colorado Medical Center
Denver, Colorado 80220

2245 **PRONK, J. C.; HOOYEN-BOSMA, E.; & EDGAR, G. W. F.** Sialic acid in erythrocytes of patients with amaurotic idiocy. *Humangenetik*, 17:65-68, 1972.

In an attempt to establish a more specific diagnostic test for amaurotic idiocy and Huntington's chorea, sialic acid was determined in the total erythrocytes and in the lipid extractable portion of erythrocytes, in order to exclude compounds which tend to distort sialic acid determinations. Material was obtained from 14 normal Ss and from 8 parents and 1 sibling of patients suffering from late infantile or juvenile forms of amaurotic idiocy, from 1 patient in the terminal phase of the disease, and from 2 patients with Huntington's chorea. The values of sialic acid in both total and lipid extracts were similar in normals and in patients. It appeared from the test, however, that the optical density at 549mu could be elevated up to five-fold by addition of $Fe^{2}+$ to the hydrolyzed lipid extract. Evidence was obtained that this elevation was due to lipid-peroxide formation. Excessive deposition of lipofuscine, which is considered to be a product of lipid peroxidation, is an essential histological characteristic of amaurotic idiocy, and hence a study of lipid peroxide

formation could prove to be of interest. (12 refs.) - *A. C. Schenker.*

Institute of Human Biology
Achter de Dom 24
Utrecht, The Netherlands

2246 SARNAT, HARVEY B.; & ADELMAN, LESTER S. Perinatal sudanophilic leukodystrophy. *American Journal of Diseases of Children*, 125(2):281-285, 1973.

Leukodystrophy is a rare neurologic disease in the newborn and may be accompanied by unusual electroencephalography. A case of sudanophilic leukodystrophy in an infant was confirmed at autopsy. Electroencephalographic patterning of asynchronous polyspike discharges, in bursts of 3 to 5 per second lasting 1 to 3 seconds alternating with 5- to 8-second periods of relative electrical silence, was noted and associated with EEG pattern characteristics found in children and young adults with certain leukoencephalitides. Myoclonic seizures which accompanied the patient's EEG discharges are also characteristic of the disease syndrome. Comparison of normal and disease-associated EEG patterns may be used as a criterion for clinical diagnosis of leukodystrophy. (34 refs.) - *C. Wares.*

University of Virginia Hospital
Charlottesville, Va. 22901

2247 HALLETT, GEORGE W. Urine VMA screening for neuroblastoma: is it worth the cost? *Pediatrics*, 51(4):757, 1973. (Letter)

In reference to Leonard et al.'s article in which the vanilmandelic acid (VMA) test strip is recommended for routine screening during the first 7 years of life for neuroblastoma, it would be worthwhile to analyze cost factors before such a program is undertaken. Cost per child would amount to $2.80. If the incidence of neuroblastoma is taken as 1:35,000 children, the cost of early discovery of one case would be $98,000. Considering the cost of retesting the false positives, this would probably come to $100,000. Even if society considers such health care affordable and justifiable, there are many other health priorities which should take precedence over such routine testing. (1 ref.) - *A. C. Schenker.*

Maine Medical Center
Portland, Maine 04102

2248 Children with cerebral palsy use symbols to "talk." *Journal of the American Medical Association*, 220(8):1055-1056, 1972.

A newly devised system of mounted symbols is enabling severely handicapped cerebral palsied children to communicate systematically for the first time with teachers and therapists. The program began initially with 10 symbols arranged on a board and a motorized pointer which could be activated by left and right levers. When the children quickly mastered the board and were able to construct a wide range of sentences, the number of symbols was expanded to 30 and then to 100. Final touches are now being put on an electronic board with 300 color-coded symbols. The most important advantage of such a system is that it enables anyone, not just close family members, to communicate with the handicapped child, thereby greatly aiding in the learning and socialization process. - *N. Mize.*

2249 HASLAM, ROBERT H. A.; BERMAN, WULFRED; & HELLER, RICHARD M. Renal abnormalities in the Russel-Silver syndrome. *Pediatrics*, 51(2):216-222, 1973.

Results of the examination of the renal system in 6 patients with Russel-Silver syndrome (RSS) are presented. Of these, 2 children have anomalies of the external genitalia, 5 have had urinary tract investigations, and in 4 of these structural abnormalities have been demonstrated by intravenous pyelogram or voiding cystourethrogram. and various anomalies of the renal tract have been noted in all the patients. It is suggested that a thorough evaluation of the renal system (for possible therapy) be carried out in all patients with RSS, as well as an 8- to 12-hour fasting blood sugar to exclude hypoglycemia. A possible explanation for the growth retardation in this condition is biologically incompetent endogenous growth hormone. (20 refs.) - *A. C. Schenker.*

The John F. Kennedy Institute
Baltimore, Maryland 21205

2250 HAGBERG, B.; OLOW, I.; & HAGBERG,

G. Decreasing incidence of low birth weight diplegia—an achievement of modern neonatal care? *Acta Paediatrica Scandinavica*, 62(2):199-200, 1973.

In an analysis of the clinical syndromes of 429 cerebral palsied Swedish children born between 1959 and 1968 and comprising a representative and unselected series, a significantly decreased total incidence of cerebral palsy ($p<0.05$) was revealed for the 5-year period 1964 to 1968. This decrease was the result of a similarly significantly lowered number of diplegic babies ($p<0.01$) and, among them, of those born prematurely with a birthweight of less than 2,500g. The introduction of new routine procedures in the care of premature babies in Sweden at this time may have been responsible for the decrease in the number of low-birthweight diplegias from the middle of the '60's. (9 refs.) - *B. J. Grylack.*

Department of Paediatrics II
Goteborgs Barnsjukhus
S-413 46 Goteborg, Sweden

2251 **KRETSCHMER, R. R.; OSUNA, M. LOPEZ; & VALENZUELA, R. H.** Reversible neutrophil defect in ataxia telangiectasia. *Pediatrics*, 50(1):147-150, 1972.

A case of ataxia telangiectasia is reported where a reversible, apparently intrinsic, neutrophil defect was detected along with some immune defects that usually accompany this syndrome. The patient, a 9½-year-old fair Mexican girl with typical cerebellar ataxia, oculocutaneous telangiectasias and sinopulmonary infections, had progressively decreasing serum immunoglobulins and somewhat defective cellular immunity as revealed by slow allograft rejection, and poor blastogenetic response to specific and nonspecific nitrogens. In addition, a reversible, apparently intrinsic, defect in phagocytic cell function was found in the absence of neutropenia. When the nitroblue tetrazolium (NBT) reduction test returned to normal in this patient, the staphylococcal abscesses of the skin also disappeared, whereas her sinopulmonary infections continued. This coincidence suggests a causal relationship, since such staphylococcal infections are unusual in ataxia telangiectasia but prominent in patients with chronic granulomatous disease where the NBT reduction test is always abnormal. (12 refs.) - *A. C. Schenker.*

Hospital de Pediatria, IMSS
Apartado Postal 73/032
Mexico 73, D. F., Mexico

2252 **ANZIL, A. P.; BLINZINGER, K.; MEHRAEIN, P.; DORN, G.; & NEUHAUSER, G.** Cytoplasmic inclusions in a child affected with Krabbe's disease (globoid leucodystrophy) and in the rabbit injected with galactocerebrosides. *Journal of Neuropathology and Experimental Neurology*, 31(2):370-388, 1972.

A study was made of the cytoplasmic inclusions found in the brain and bone marrow biopsies from an infant with globoid leukodystrophy and induced locally in 4 young adult rabbits by intracerebral and epidural injection of beef brain galactocerebrosides. Experimental observations and review of the literature indicate that the cytoplasmic inclusions found in patients with globoid leukodystrophy can be very pleomorphic. The inclusions seen in the bone marrow macrophages were quite distinct from those in the brain biopsy, whereas inclusions induced experimentally were generally identical with those found in human brain tissue, regardless of the site of injection. Despite reports to the contrary, it appears that inclusions in Krabbe's disease can occur within membrane-bound lysosomal structures as well as free in the cytoplasm of cells. Ultrastructurally, it is the inclusions themselves, despite their pleomorphism, and not the cells containing them, which are the hallmark of Krabbe's disease. The name aciculate cell (aciculocyte) is the preferred descriptive designation for the storage cell. The masses of microvilli and the presence of cellular bridges in the animal data demonstrate that polykaryocytes, at least experimentally, originate by cell fusion rather than by nuclear fission. (38 refs.) - *B. J. Grylack.*

Max-Planck-Institut fur Psychiatrie
D-8000 Munich 23, Federal Republic of Germany

2253 **ADORNATO, BRUCE T.; O'BRIEN, JOHN S.; *LAMPERT, PETER W.; ROE, THOMAS F.; & NEUSTEIN, HARRY B.** Cerebral spongy degeneration of infancy: a biochemical and ultrastructural study of affected twins. *Neurology*, 22(2):202-210, 1972.

Mitochondrial abnormalities and biochemical assay

findings are described in dizygotic twin girls with spongy degeneration. Direct quantitation of Na-K-MG-stimulated adenosine triphosphatase (ATPase) and cytochrome oxidase, using fresh homogenates from the biopsy specimen of the nondominant frontal cortex and adjacent subcortical white matter, failed to disclose any abnormality in their activities, thus proving that an enzyme defect in the ionic pump was not involved in these cases. Striking abnormalities were seen in the mitochondria of the biopsy specimen, which showed spongiform changes. The presence of peculiar filaments and electron dense deposits in the mitochondria and distended, separated myelin lamellae and increased cellular space in spongy subcortical white matter was seen. An explanation for the morphologic appearance of astrocytic mitochondria is presently lacking. Proposed explanations for the unusual pattern within the mitochondrial matrix range from accumulations of abnormal lipoproteins or other metabolites to a physiologic ordering of the mitochondrials cristae in the process of electron transfer. (26 refs.) - *A. C. Schenker.*

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San Diego, La Jolla, California 92037

2254 **PENNEY, J. B., JR.; WEINER, L. P.; HERNDON, R. M.; NARAYAN, O.; & JOHNSON, R. T.** Virions from progressive multifocal leukoencephalopathy: rapid serological identification by electron microscopy. *Science*, 178(4056):60-61, 1972.

A method of serologic identification of virions, extracted directly from diseased tissues of the brain of a patient with progressive multifocal leukoencephalopathy (PML), is described. Electron microscopy of the white matter from the brain of a patient with PML (patient A) revealed virions. Virions isolated directly from patient A's brain homogenate were treated with antiserum to SV 40, with rabbit antiserum to previous PML isolates, or with serum from patient B (with PML). Serum from patient A did not react with virions from her brain as well as with other viruses; this confirms previous neutralization tests that failed to demonstrate antibody in this serum. Serum of patient B did agglutinate these virions as well as previous isolates and SV 40. The reactions demonstrate that the particles in the patient's brain were antigenically related to SV 40. The reactions of antiserum with virions from brain confirm the isolation studies and indicate that the SV 40-like antigenic phenotype did not result from recombination with latent simian agents in cell cultures. The lack of cross-reaction with polyoma also confirms the specificity of this method. Immune electron microscopy may have the potential to distinguish very rapidly antigenically distinct virions extracted directly from brains of patients with PML. (5 refs.) - *A. C. Schenker.*

Johns Hopkins University School of Medicine
Baltimore, Maryland 21205

2255 **HILLENBRAND, PEGGY.** The physician, education and the handicapped child. *Clinical Proceedings, Children's Hospital National Medical Center*, 28(5):139-140, 1972. (Letter)

Reference is made to an editorial by Eng on the dilemma of available facilities for the management of the handicapped child in this country. The Cerebral Palsy Development Center in Falls Church in Northern Virginia has a superior program with a multidisciplinary approach. This includes a program where parents are given guidance in a constructive home program and children are seen in individual therapy according to need. There are one-half day classes for 3-year-olds and all-day classes for 4- and 5-years-olds. An evaluation clinic is held monthly by an orthopedist. The Center is operated by a volunteer Board of Directors, an administrator, and a school director. The staff is a highly trained group of professionals. Volunteers serve as classroom aides, transport children to school, and assist with clerical work and fund raising. This type of facility can serve as a model on a national level. - *A. C. Schenker.*

Cerebral Palsy Development Center of
North Virginia
111 North Cherry St.
Falls Church, Virginia 22046

2256 **HIROSE, GENJIRO; & BASS, NORMAN H.** Metachromatic leukodystrophy in the adult: a biochemical study. *Neurology*, 22(3):312-320, 1972.

To provide information on the pathogenesis of metachromatic leukodystrophy (MLD) microchemical analyses of sural nerve were conducted on a

26-year-old woman with this disease. The results were compared with the classical infantile form of the disease. The pedigree suggests an autosomal recessive mode of inheritance. The patient showed absent arylsulfatase A activity similar to that found in the infantile form, 10.9 nM of 4-nitrocatechol released per hour/mg protein. Sections of sural nerve showed myelin degeneration of the segmental type in both adult- and infantile-onset MLD; both pathologic specimens, examined with Hirsch-Peiffer stain, revealed abundant metachromatic granules in the tissue and within both Schwann cells and macrophages. DNA increased by approximately 15% in both specimens, but RNA was increased by 12% only in the adult form. Cholesterol was decreased by 13 and 20% in infantile and adult MLD, respectively. Total galactolipids were decreased by 21% in infantile onset only. A reversal of the cerebroside:sulfatide ratio from a normal value (3.4±0.3) to mean values of 0.8 and 0.2 for infantile- and adult-onset MLD, respectively, was found. It is postulated that the clinical variants reported for this disease, characterized by later onset, result from an absence of the heat-labile component of cerebroside sulfatase superimposed upon a genetically related ability of oligodendroglia and Schwann cells to maintain the myelin sheath by the enzymatic induction of nonspecific sulfatases. (48 refs.) - *A. C. Schenker.*

University of Virginia School of Medicine
Charlottesville, Virginia

2257 SANDBANK, U.; & LERMAN, P. Progressive cerebral poliodystrophy-Alper's disease. *Journal of Neurology, Neurosurgery, and Psychiatry*, 35(6):749-755, 1972.

Two siblings had seizures at 1 mo, progressive spasticity, MR, and died at 6 and 18 mo of bronchopneumonia. Brain biopsy of a third 3-mo-old female sibling revealed normal cortex at low magnification, but electron microscopy revealed alterations in the neuronal perinuclear mitochondria. The mitochondria were either enlarged with short or absent cristae, or normal sized with electron dense particles adhering to the inner membrane, or degenerating. At autopsy (age 15 mo), the brain was small (480g); the cortex was completely disorganized with neurons absent and a massive proliferation of astrocytes and microglia. The cerebellum had neuronal loss, while the stem, pons, medulla, and cord appeared normal. Altered neuronal mitochondria were found in other cases of repeated seizures, chromatolysis due to axonal lesion, and X-irradiation of the brain, and may be either reactive or a result of a familial disorder. The cases here may have had an idiopathic type of Alper's disease. (25 refs.) - *V. J. Goldberg.*

Belinson Hospital
Tel Aviv, Israel

2258 GROVER, WARREN D.; AUERBACH, VICTOR H.; & PATEL, MULCHAND S. Biochemical studies and therapy from early infancy in subacute necrotizing encephalomyelopathy. *Neurology*, 22(4):428, 1972. (Abstract)

The course of subacute necrotizing encephalomyelopathy (SNEM) was followed in an infant whose brother was found to have the disease in a postmortem examination. Observations were begun when the infant was 8 mos old. Early findings included: an abnormal macular appearance, elevated blood lactic acid, and elevated cerebrospinal proteins before the onset of clinical symptoms. After clinical signs appeared, high plasma alanine levels and renal tubular acidosis were established. Administration of biotin, lipoic acid, and thiamine produced no clinical effect. Slight decreases in blood lactic acid and plasma alanine were observed during the disease course. Pyruvate carboxylase activity in hepatic tissue (obtained by biopsy) was in the low average range, but the levels of enzyme activity of brain, liver, and kidney pyruvate carboxylase obtained at autopsy were markedly diminished. Thiamine triphosphate content was low at various levels of the neural axis. It is suggested that the decreased levels of cerebral and hepatic pyruvate carboxylase are a secondary effect and not the primary cause of SNEM. - *A. C. Schenker.*

2259 FESTOFF, B. W.; & KRAEMER, K. H. Xeroderma pigmentosum: neurological and cutaneous abnormalities associated with a defect in DNA repair. *Neurology*, 22(4):420, 1972. (Abstract)

Neurological abnormalities in association with xeroderma pigmentosum (XP) are reported in 2 female siblings. The findings include microcephaly, MR, choreoathetoid movements and nerve deafness, and the unique finding of total areflexia, despite normal strength. On examination for a

diffuse neuropathy, delayed motor nerve conduction velocities, neuropathic electromyogram, and fiber-type groupings in muscle were found. Both patients showed approximately 35% of normal ultraviolet-stimulated tritiated thymidine incorporation into their lymphocytes. The patients had a chronic neuropathy with evidence of collateral reinnervation. Inefficient DNA repair of neurons or Schwann cells may be involved in this neuropathy. - *A. C. Schenker.*

2260 **TRUSWELL, A. STEWART; & PFISTER, PETER J. V. S.** Cerebrotendinous xanthomatosis. Medical memoranda. *British Medical Journal*, 1(5796):353-354, 1972.

A S. African woman had symptoms compatible with cerebrotendinous xanthomatosis, including MR (possibly of late onset), cerebellar ataxia, increased deep reflexes, juvenile cataracts, massive tendon xanthomas, and minimally raised serum cholesterol. In this rare disease (9 other cases described), probably mendelian recessive, tendon xanthomas are not an indication of hypercholesterolemia. (5 refs.) - *V. J. Goldberg*

Queen Elizabeth College
London, W8 7AH England

2261 **DONNER, M.; WALTIMO, O.; PORRAS, J.; FORSIUS, H.; & SAUKKONEN, A.-L.** Subacute sclerosing panencephalitis as a cause of chronic dementia and relapsing brain disorder. *Journal of Neurology, Neurosurgery, and Psychiatry*, 35(2):180-185, 1972.

Two cases of subacute sclerosing panencephalitis (SSPE) which resulted in partial remissions are described. A 20-year-old woman had initial symptoms at age 8 of nocturnal convulsions, and mental slowness (IQ 68). At age 10 there were falling fits and mild MR (IQ 83), while pneumoencephalography was normal. After age 13 (IQ 74), the convulsions were less frequent. At age 19, she had IQ 59, difficulties with body image, mental confusion, and cerebrospinal fluid antibody to measles virus. An 11-yr-old boy had initial symptoms at age 7 of jerks, behavior difficulties, and stumbling. Within 2 mo, he had varicella, rigidity of the left arm, uncertain coordination tests, staggering gait, and inability to understand speech. One yr later he became drowsy, incontinent, and unable to turn in bed. Within 1 mo, signs of remission became apparent and he learned to walk, form sentences, and become continent; the jerks and absences ceased. The measles antibody titers at that time were 1:16 in the cerebrospinal fluid and 1:512 in serum. At age 11 he has IQ 58 and near normal coordination tests, muscle tone, and tendon reflexes, but poor WISC performance tests. During the quiescent stage there are high measles antibody titers and the EEG findings are not reliable. The relapsing of case 1 shows that the disease is probably latent during the recovery phase. Of 23 cases of SSPE, 5 were fatal, 15 were chronic (3 of these had short-lived remissions), 1 is new, and 2 show apparent recovery. (17 refs.) - *V. J. Goldberg.*

University of Helsinki
Helsinki, Finland

2262 **KORNFELD, MARIO.** Generalized lipofuscinosis (Generalized Kuf's disease). *Journal of Neuropathology and Experimental Neurology*, 31(4):668-682, 1972.

A 26-yr-old woman suffered from progressive cerebellar ataxia and mental impairment. At autopsy, neurons with swollen bodies and finely granular eosinophilic cytoplasm were found throughout the central nervous system, with the deeper layers of the cortex, striatum, globus pallidum, and diencephalic ganglia most extensively involved. Scattered focal loss of Purkinje cells was observed in the cerebellum. The Purkinje cells were enlarged and contained either fine eosinophilic or coarse yellow granules. Swollen cells with granular cytoplasm were found in liver, kidney, spleen, bone marrow, lung, and mesenteric plexus. Electron microscopy of neuronal tissue revealed large numbers of irregular bodies with all the features of lipofuscin in the perikarya. Lysosome-like bodies in the cytoplasm tended to aggregate around the lipofuscin particles and there were increased numbers of mitochondria. Lipofuscin bodies were identified in the cerebellum, thalamus, spleen, and liver. The lipofuscin granules consisted of a single membrane enveloping globular electron-lucent material which contained osmophilic granules, short bands, or (in Purkinje cells) stripes. These findings are unusual because of the absence of lamillar bodies usually found in lipid storage diseases such as Niemann-Pick or Tay-Sachs. There are resemblances to Kuf's disease, except that lipofuscin particles in the viscera have been reported in only two cases. The lipofuscinosis may represent a new entity or it may be

secondary to another defect. (34 refs.) - *V. J. Goldberg.*

University of New Mexico School of Medicine
Albuquerque, N. M.

2263 **WITZLEBEN, CAMILLUS L.** Lymphocyte inclusions in late-onset amaurotic idiocy. Value as a diagnostic test and genetic marker. *Neurology*, 22(10):1075-1078, 1972.

The finding of similar complex inclusions in the lymphocytes of a 7-year-old boy with the clinical and pathologic features of late-onset amaurotic idiocy, a younger clinically affected sibling, and their parents indicated the usefulness of electron microscopy in diagnosing this condition and in facilitating recognition of carriers of the form of late-onset amaurotic idiocy present in this family. The inclusions, ranging from dense, apparently homogenous, osmiophilic inclusions to laminar and apparent tubular profiles in the propositus, were less numerous but comparable in the mother and father. These data, together with observations made by others that the characteristic "asurophilic" granules found in the granulocytes from affected patients are also found in evident carriers of the condition, raise the possibility that abnormal neuronal storage might also be present in carriers, apparently without having any marked functional effect. (2 refs.) - *B. J. Grylack.*

St. Louis University School of Medicine
St. Louis, Missouri 63104

2264 **CARPENTER, STIRLING; KARPATI, GEORGE; & ANDERMANN, FREDERICK.** Specific involvement of muscle, nerve, and skin in late infantile and juvenile amaurotic idiocy. *Neurology*, 22(2):170-186, 1972.

A series of 9 cases is presented of amaurotic idiocy or cerebral lipidosis in the late infantile and juvenile age range. The morphological findings in cases 1 through 4 (all in the late infantile age range) as well as the evolution of the disease are similar: accumulation of cytosome curvilinear profiles (CCPs) in a great variety of tissues. Cases 8 and 9, also in the late infantile range, appear to form a transitional category between the late infantile category with CCPs and the juvenile with cytosome and fingerprint profiles (CFPs). The morphological findings in cases 5, 6, and 7 (in the juvenile age range) are similar, but the degree of smooth and skeletal muscle involvement varies considerably among them. CFPs were found in neurons, Schwann cells, eccrine sweat gland cells, and endothelial and smooth muscle cells; these were not seen in the skeletal muscle, despite the very marked involvement of this cell type with cytosome rectilinear profiles (CRPs). CCPs and CRPs were demonstrated in the skeletal muscle by electron microscopy; these were distinct from any cytosome occurring in skeletal muscle in other neuromuscular disease. Cytosomes similar to those found in the neurons were found in the eccrine sweat glands. On the basis of these studies, it is suggested that electron microscopy affords the best means of classifying these cases; CFPs, CCPs, and CRPs are ultrastructurally distinct from normal human neuronal lipofuscin. (35 refs.) - *A. C. Schenker.*

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Montreal 112, Canada

2265 **HABERLAND, CATHERINE; BRUNNGRABER, E. G.; WITTING, L. A.; & HOF, H.** Late infantile amaurotic idiocy (LIAI): anatochemical report of a case. *Neurology*, 22(3):305-311, 1972.

Clinical, histopathological, and biochemical findings in a 10-year-old boy with late infantile amaurotic idiocy (LIAI) are reported; the clinical and histopathological features resembled the Jansky-Bielschowsky type of LIAI. There was a significant decrease in the amount of gangliosidic N-acetylneuraminic acid (NANA) recovered from the gray matter; the decrease in ganglioside content of white matter was less marked. The chloroform-rich lower phase obtained after partitioning of the gangliosides contained no hexosamine; white and gray matter yielded 17.3 and 2.9 micro-M of cerebroside galactose/gm of brain tissue, respectively. The NANA-free glycopeptides of small molecular size were markedly reduced or absent. A lack of ganglioside involvement in the lipid storage is suggested as the primary factor in the neuronal losses in the case presented. The low cerebroside content supports the observation that reduction in myelin lipids in white matter may occur despite morphologically normal myelination. The most marked abnormality appears to be a total loss of the NANA-free glycopeptides of

smaller molecular size. Other variants of LIAI are reviewed. (41 refs.) - *A. C. Schenker.*

Illinois State Psychiatric Institute
Chicago, Illinois 60612

2266 **HULTBERG, BJORN; & OCKERMAN, PER ARNE.** Urinary excretion of amino acids in juvenile amaurotic idiocy. *Metabolism*, 21(3):231-234, 1972.

An evaluation of urinary amino acids in juvenile amaurotic idiocy using the Technicon amino acid analyzer is presented which is in disagreement with other published results in this disease. The subjects comprised 6 female patients (age 8-17 years) and 12 male patients (age 9-22 years), with confirmed amaurotic familial idiocy, and the controls were those described in a previous publication. Amino acid determinations were performed by the King method, using a Technicon analyzer, and compared with standards. No systematic significant differences were found between urinary amino acids in patients and in controls. In one patient the level of carnosine was slightly elevated, and no abnormal peaks were found in the patients where 1-methylhistidine was eluted. The negative findings may be due to the difficulty in diagnosing juvenile amaurotic idiocy, and positive results described by others may be associated with a different disease. Another possibility of error in the results may be due to the vitamin E status. Artifacts in the analysis should be considered. The finding of imidazoluria in juvenile amaurotic idiocy may be a secondary finding and not representative of the primary defect. (10 refs.) - *A. C. Schenker.*

University Hospital
Lund, Sweden

2267 **WILSON, JOHN.** Tapetoretinal degeneration. *British Medical Journal*, 1(5797):443, 1972. (Letter)

Four patients with unrecognized visual failure and accompanying behavioral disturbance probably suffered from an organic dementia, of which fluctuating behavioral problems are only one aspect. Tapetoretinal degeneration is the most common presenting feature of Batten's disease, the juvenile form of so-called amaurotic family idiocy, and a diagnosis of this disease must be considered in any patient of school age who develops a tapetoretinal degeneration, especially in association with behavioral problems. - *B. J. Grylack.*

Hospital for Sick Children
London W.C.1, England

2268 **GOODWIN, A. W.** Continuous positive airway pressure in respiratory distress syndrome. *Lancet*, 1(7758):1019-1020, 1972. (Letter)

Recent experiments with a modified 'Pneumask' reaffirm that a pressure recorder measuring directly from the head box is essential in all systems for applying continuous positive airway pressure to infants with respiratory distress. Only in that way is it possible to know just what pressure is being applied to the airway. Additionally, it should be considered whether the benefit from the head mask might come from the pressure exerted by the neck seal in partially obstructing the airway—thereby functioning in a manner similar to the glottis—rather than from the inspired pressure. (2 refs.) - *N. Mize.*

London Hospital Medical College
London E.1, England

2269 **DAVID, T. J.** Palmar dermatoglyphs in tuberous sclerosis. *Journal of Medical Genetics*, 9(4):443-447, 1972.

The palmar dermatoglyphs of 54 patients with tuberous sclerosis, which is inherited as an autosomal dominant condition, were compared with those of 500 male and 500 female controls. Rolled and plain impressions were obtained from all fingers, and 3 sets of palm prints were recorded. Of 165 statistical comparisons there were 3 significant findings, 2 at $p<0.025$ and 1 at $p<0.05$. Two involved fingerprint pattern trends in female patients, but the male patients showed opposite

tendencies. The third positive result was a small decrease in the summed a-b ridge count, significant at $p<0.05$ in the males. Unless these 3 trends can be confirmed in other patients with tuberous sclerosis, it must be concluded that no specific palmar dermatoglyphic features are associated with it. (14 refs.) - *B. J. Grylack.*

General Hospital
Bristol, England

2270 **MUTCHINICK, OSVALDO.** A syndrome of mental and physical retardation, speech disorders, and peculiar facies in two sisters. *Journal of Medical Genetics*, 9(1):60-63, 1972.

Two sisters born to consanguineous parents appeared to be affected with a new syndrome of MR and multiple congenital anomalies. The almost identical clinical picture presented by the 2 propositа was characterized by SMR, slow physical development, microbrachycephaly, peculiar facies, pigeon chest, congenital heart disease, nonspecific renal malformations, and some degree of generalized melanin defect, as suggested by the very light white skin, blond hair, and severe photophobia. The existence of a mongoloid sib and some facial features of the 2 affected girls raised the possibility of a balanced translocation in 1 parent involving a G-group chromosome, with a partial trisomy in the mongoloid sib and a deletion of a G chromosome in the 2 affected sisters. No chromosomal abnormalities were detected, however. The observed clinical picture shared some features with true recessive microcephaly and Seckel's bird-headed dwarfism, but the whole appearance of the face, prognathism, severe photophobia, pigeon chest, and cardiac and renal malformations were evidence of a different entity. An autosomal recessive inheritance is proposed for this syndrome. (6 refs.) - *B. J. Grylack.*

Medical Genetics Center
Buenos Aires, Argentina

2271 **FEDRICK, JEAN; & BUTLER, N. R.** Hyaline-membrane disease. *Lancet*, 2(7780):768-769, 1972. (Letter)

Careful examination of the data of the 1958 British Perinatal Mortality Survey, involving the events of pregnancy and delivery of approximately 7,117 singleton stillbirths and neonatal deaths over a 3-month period, has shown the incidence of hyaline membrane disease among infants delivered by cesarean section before the onset of labor to be greater than that among infants delivered abdominally during labor. The total incidence among live infants delivered by section before labor started was 46 per 1,000 as compared with only 3 per 1,000 among infants delivered abdominally after the commencement of labor and 2 per 1,000 among infants delivered *per vaginam*. When gestation was taken into account, the contrast in incidence among the 3 groups was still apparent. The findings support the theory that lung surfactant is related to the production of labor inducing corticosteroids by the fetus. (6 refs.) - *B. J. Grylack.*

Department of Regius
Professor of Medicine
Oxford, England

2272 **MIRHOSSEINI, S. ALI; HOLMES, LEWIS B.; & WALTON, DAVID S.** Syndrome of pigmentary retinal degeneration, cataract, microcephaly, and severe mental retardation. *Journal of Medical Genetics*, 9(2):193-196, 1972.

Two SMR brothers aged 28 and 24 years presented with pigmentary retinal degeneration, cataracts, arachnodactyly, hyperextensible joints, mild scoliosis, and microcephaly due apparently to a previously undescribed and presumably hereditary disorder. One brother also had hypogonadism. Although the particular combination of physical abnormalities observed seemed to be unique, some of these features have been reported in other hereditary disorders. (15 refs.) - *B. J. Grylack.*

Massachusetts General Hospital
Boston, Massachusetts

2273 **BARTSOCAS, CHRISTOS S.; & PAPAS, CONSTANTINE V.** Popliteal pterygium syndrome. Evidence for a severe autosomal recessive form. *Journal of Medical Genetics*, 9(2):222-226, 1972.

Four children in the same family were severely affected with the popliteal pterygium syndrome. The proposita presented with MR, absent corneae, multiple webs, cleft palate, micrognathia, syn-

dactyly of fingers and toes with hypoplastic or absent phalanges and nail aplasia, hypoplastic labia majora, and a bicornuate uterus, and she died at age 9 weeks. All other affected sibs demonstrated similar anomalies and died within the first week of life. The 35-year-old mother and 39-year-old father, third cousins, were both healthy, and no malformations had been reported in the family for at least 3 generations. The many anomalies and MR present in some cases provided evidence for a severe autosomal recessive mode of inheritance for this family. (26 refs.) - *B. J. Grylack.*

'Aghia Sophia' Children's Hospital
Athens 608, Greece

2274 **YARNELL, PHILIP R.; MATIN, PHILIP; & CUNNINGHAM, JAMES G.** Canine radioisotope cisternography. Implications for hydrocephalus study. *Neurology*, 22(8):806-809, 1972.

The use of radioiodinated human serum albumin cisternography with 3 normal 15- to 21-month-old beagles and 1 12-month-old poodle with a progressive communicating hydrocephalus demonstrated that the cerebrospinal fluid flow pattern was along the base of the brain into the subfrontal region in all experimental animals. The main differences seen in the hydrocephalic dog were the greater size of the central void between the cisterna magna and olfactory cisterns at 2 to 4 hours after injection and the lack of detection of olfactory or optic cisterns at 24 and 48 hours. Since the pathway of cerebrospinal fluid flow in dogs differs markedly from that in man, caution should be applied when the dog is used as a model for human states of cerebrospinal fluid pathology. (12 refs.) - *B. J. Grylack.*

Denver General Hospital
Denver, Colorado 80204

2275 **JAMES, JOHN A.** Respiratory distress syndrome. *American Journal of Diseases of Children*, 124(8):296, 1972. (Letter)

The suggestion that the predisposition to severe lower respiratory tract disease seen upon follow-up of premature infant survivors of the respiratory distress syndrome during the newborn period represented a late consequence of the syndrome cannot be supported, in the absence of a control group of infants who did not have the syndrome. The long-term prognosis of the syndrome justifies a carefully controlled study. (2 refs.) - *B. J. Grylack.*

2276 **EMANUEL, IRVIN.** Non-tuberous neural-tube defects. *Lancet*, 2(7782):879, 1972. (Letter)

Despite a proposal that an as yet undefined specific chemical associated with the potato blight is the teratogen responsible for anencephalus and spina bifida, the similarity in incidence rates of neural-tube defects in countries with great differences in potato production and consumption does not appear to support this hypothesis. Of all the epidemiologic relationships in anencephalus and spina bifida, the social-class effect is the most striking and constant, excesses of neural-tube defects being seen among the poorer elements of the population in Taiwan as well as in the United Kingdom, the United States, Canada, and Israel. It is unlikely that the social-class relationship in neural-tube defects in Taiwan can be attributed to a potato-associated teratogen, and it is probable that the same factors produce the social-class relationship wherever it is seen. (12 refs.) - *B. J. Grylack.*

University of Washington
Seattle, Washington 98195

2277 **OUTERBRIDGE, EUGENE W.; & STERN, LEO.** Respiratory distress syndrome: reply by authors. *American Journal of Diseases of Children*, 124(8):296, 1972. (Letter)

A group of infants with repeated attacks of bronchiolitis occurring at a relatively early age and with sufficient severity to necessitate respirator management in some cases was associated with an alarmingly frequent antecedent history of respiratory distress syndrome. The incidence was much greater than that anticipated from the known rates for the syndrome in premature infants. The fact that the only 3 children in this group requiring mechanical ventilation were respiratory distress syndrome survivors was more than coincidental. (1 ref.) - *B. J. Grylack.*

2278 **HART, MICHAEL NOEL; MALAMUD, NATHAN; & ELLIS, WILLIAM G.** The

Dandy-Walker syndrome. A clinicopathological study based on 28 cases. *Neurology*, 22(8):771-780, 1972.

Study of the pathological findings in 28 autopsied cases of the Dandy-Walker syndrome indicated that hydrocephalus, cerebellar vermis aplasia or hypoplasia, and enlargement of the fourth ventricle with a posterior fossa cyst are the essential constituents of the syndrome. However, other central nervous system and systemic anomalies formed a part of this complex in 68% of cases, a factor which suggested that the entire group of anomalies comprises a more general developmental disturbance. The findings indicated that failure of the foramina to open cannot be solely responsible for the observed pathology of the cerebellum of these individuals. The data supported the concept of the Dandy-Walker syndrome as part of a complex maldevelopment initiated very early in fetal life and due most likely to intraventricular accumulation of excessive prechoroidal cerebrospinal fluid. (30 refs.) - *B. J. Grylack*.

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Washington, D.C. 20305

2279 Hyaline membrane disease: the era of CPAP, CNP and PEEP. *Canadian Medical Association Journal*, 106:1150-1151, 1972. (Editorial)

Recent attempts to combat the increased retractive force of the lung of infants with hyaline membrane disease have led to a remarkable advance in the treatment of the disease. Provision of a constant positive airway pressure (CPAP) of 5 to 20 cm H_2O via an endotracheal tube while allowing the infant to breathe spontaneously, use of a constant negative pressure (CNP) around the thorax of spontaneously breathing infants, and use of a positive end expiratory pressure (PEEP) or continuous positive pressure breathing represent the treatment of choice at the present time. (10 refs.) - *B. J. Grylack*.

2280 **EMANUEL, IRVIN.** Spina bifida, anencephaly, and potato blight. *Lancet*, 2(7790):1308-1309, 1972. (Letter)

A potato-associated factor cannot possibly be important for the spina bifida and anencephaly cases seen in Taiwan. The neural-tube defects diagnosed in a recent Taiwan study are clinically the same as and share the same striking socioeconomic effect seen in neural-tube defects in other countries. The approximately even sex distribution for anencephaly is not unique to Taiwan and cannot be considered an indicator of incorrect diagnoses in that study. Teratological experimentation on potato blight in marmosets has generally yielded results which are uninterpretable with reference to specific etiologies of human malformations. No direct evidence is available which implicates a specific teratogen, potato or otherwise, in anencephaly and spina bifida, and the indirect epidemiologic evidence is only tenuous. Criticism of hypotheses linking teratogens to anencephaly and spina bifida cannot be dismissed easily until these hypotheses are tested directly. (13 refs.) - *B. J. Grylack*.

Department of Epidemiology and
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University of Washington SC-36
Seattle, Washington 98195

2281 **SYMON, LINDSAY; DORSCH, N. W. C.; & STEPHENS, R. J.** Pressure waves in so-called low-pressure hydrocephalus. *Lancet*, 2(7790):1291-1292, 1972.

Continuous measurement of intracranial pressure over several days in 18 cases revealed increases of pressure during nocturnal sleep in some patients with communicating hydrocephalus, whereas other patients with signs and symptoms of the syndrome did not demonstrate this phenomenon. "Episodically raised pressure hydrocephalus" may be a more appropriate term for so-called low-pressure hydrocephalus. An explanation for these episodes might be that in a critically balanced equilibrium between production and resorption of cerebrospinal fluid, transient changes in intracranial blood-volume during sleep, for example, could disturb the equilibrium of the intracranial pressure and result in a wave of increased pressure. Equilibrum could be restored to normal either by hyperventilation or by some adaptation of intracranial blood-volume. Correlation of intracranial pressure of resorptive capacity in communicating hydrocephalus with the reaction of patients to shunting is in progress. In 2 of 10 cases, both with pressure waves, complicating subdural hygromata developed subsequent to shunting and resolved without severe disability; of the group as a whole, however, only 5 patients could be considered

unequivocally improved, 1 of them only after prolonged treatment of the hydrocephalus and subdural hygromata. (7 refs.) - *B. J. Grylack.*

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2282 **MASSACHUSETTS DEPARTMENT OF HEALTH.** New regulations for newborn services. *New England Journal of Medicine,* 286(25):1363-1364, 1972. (Editorial)

New regulations governing neonatal service effective since September 15, 1970, emphasize the diagnosis and treatment of "special care" infants, including those with respiratory distress, congenital anomalies, jaundice, seizures, infections, or other immediately threatening conditions. Maternity services delivering 2,000 or more infants per year, or those with a daily census of 4 low-birth-weight infants must provide special (intensive) care nurseries. Smaller services must submit plans to the Department of Public Health for special-care management, including plans for transfer of patients to specialized nurseries. Some nurseries are designated as transfer nurseries, and more than 600 neonates have been transferred for special care in 1970. - *V. J. Goldberg.*

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Boston, Massachusetts 02116

2283 **LARROCHE, JEANNE-CLAUDIE.** Post-haemorrhagic hydrocephalus in infancy: anatomical study. *Biology of the Neonate,* 20:287-299, 1972.

Nine anatomicoclinical observations of prematurely born infants with posthemorrhagic hydrocephalus who survived from 8 to 49 days illustrate the multiple sources of hemorrhages, their pathways, and the mechanisms of acquired hydrocephalus in the neonatal period. It was shown that the initial bleeding and the exact location of the blockage could be anatomically identified with precision. In most cases the obliterative arachnoiditis in the posterior fossa blocked the normal cerebrospinal fluid pathways, but in 1 case the blockage was already in the upper part of the aqueduct of Sylvius. Diagnosis of hydrocephalus is very difficult in the neonatal period. In 7 of 9 cases the diagnosis of intracranial hemorrhage was made; 5 infants only exhibited an increase in head circumference. (10 refs.) - *B. J. Grylack.*

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F-75 Paris 14e, France

2284 **STAHLMAN, M.; BLANKENSHIP, W. J.; SHEPARD, F. M.; GRAY, J.; YOUNG, W. C.; & MALAN, A. F.** Circulatory studies in clinical hyaline membrane disease. *Biology of the Neonate,* 20:300-320, 1972.

Various cardiovascular parameters of 168 infants with hyaline membrane disease were measured to provide information on the mechanisms governing marked sequential changes from the moment of birth. The mortality rate was 32%. Aortic pressure increased gradually in survivors. Lowered systemic blood pressure in some sick infants may have been brought about by hypovolemia or myocardial depression. Of 18 infants with hypertension on at least a single occasion, 11 died, their mean pressure/kg being higher early in the disease course than that of the survivors. Shunting through the foramen ovale occurred largely, if not exclusively, from the inferior vena cava directly into the left atrial cavity. There were statistically significant increases in the height of both a and v waves in both the inferior vena cava and left atrium in infants 13 to 36 hours of age as compared with those pressures at 12 hours or less. A pattern of predominately right-to-left shunting in the early hours after birth was found to change gradually to one of predominately left-to-right shunting as the infant began to recover, most of the sickest infants having died by this time period. The data and evidence from the literature suggested that significant right-to-left ductal shunting rarely occurs after the first few hours except in extremely ill infants whose PO_2 are low enough to produce marked elevation of pulmonary vascular resistance. Marked acidosis may also play a role in this event at somewhat higher PO_2. (21 refs.) - *B. J. Grylack.*

Vanderbilt University School of Medicine
Nashville, Tennessee 37232

2285 **KARCH, S. B.; & URICH, H.** Occipital encephalocele: a morphological study. *Journal of the Neurological Sciences,* 15(1):89-112, 1972.

Details of morphological abnormalities encountered in 5 infants with large occipital encephalo-

celes are described. The sample material was taken from 5 patients, all female, who died within 18 weeks of birth; 4 of these infants manifested defective temperature regulation during life. The results revealed that this condition is a complex malformation involving various parts of the neuraxis and its mesenchymal coverings. Details are given of the morphological findings in the skull, cerebral hemispheres, ventricular system, basal ganglia, optic pathway, commissural system, hypothalamus, brainstem, cerebellum, and spinal cord. The point that emerges from physiological and morphological studies is that infants with disturbances of central autonomic control have malformations too severe to be amenable to surgery. Despite the apparently normal cellularity of the anterior hypothalamic gray masses, it is possible to exclude structural derangements in the presence of gross malformations in the region of the lamina terminalis. It is probable that hypoplasia of the pyramidal tracts, seen in extreme form in the material presented, may be present to a lesser degree in a proportion of the operable cases. (32 refs.) - *A. C. Schenker.*

The London Hospital
London, E.1, England

2286 DEUEL, RUTHMARY K. Polygraph monitoring of apneic spells. *Archives of Neurology*, 28(2):71-76, 1973.

Respirations, ECGs, eye movements, and skeletal muscle tone were recorded in infants to determine whether apnea and periodic respirations were correlated with either any EEG abnormalities or any one stage of sleep. The Ss were 5 infants with severe apneic spells and 8 premature infants with no clinically apparent apnea. In each of the patients, at least a few respiratory pauses were recorded, all of less than 20 seconds' duration. Apneic episodes or respiratory pauses over 20 seconds' duration were recorded in 3 patients; the first was an infant who had periodic breathing at other times, and appeared to differ from a typical respiratory pause of that infant only in length; the second was a probable seizure; and the third appeared only after preliminary evidence of cerebral anoxia, secondary to hypoxemia. The recordings support the finding that over 20% of respiratory epochs of each premature below 36 weeks' gestational age is periodic; it is suggested that periodic and irregular respirations are normal physiological phenomena in premature infants. No inverse correlation could be found of postconceptional age, weight, and EEG maturation with the number and duration of respiratory pauses. (19 refs.) - *A. C. Schenker.*

University of Chicago Hospitals
Chicago, Illinois 60637

2287 AFIFI, A. K.; REBEIZ, J.; MIRE, J.; ANDONIAN, S. J.; & DER KALOUSTIAN, V. M. The myopathology of the prune belly syndrome. *Journal of the Neurological Sciences*, 15(2):153-165, 1972.

Light and electron microscopic myopathology in a female with the rare disorder called the prune belly syndrome is described. The patient was an 8-month-old female who had symmetrical swelling of both sides of the abdomen accentuated by coughing or crying. The microscopic studies were performed on muscle biopsy obtained from the rectus abdominis. The light microscopic findings gave evidence of an active disease process characterized by segmental muscle fibre necrosis without regeneration. The electron microscopic observations point to some similarities between the cytological alterations seen in muscle in the prune belly syndrome in central core disease and congenital muscular dystrophy. The changes comprised variations in fibre size, fibre necrosis, an increase in sarcolemmal nuclei, the presence of capillaries within muscle fibres, excessive collagen accumulation, Z-line abnormalities, sarcoplasmic reticulum dilatation, and myofilamentous disarray and loss. It is likely that a genetically determined congenital type of myopathy is the basis of the myopathology of this syndrome, which may also include midgut malrotation, chest wall deformities, anomalies of lower extremities, cardiac anomalies, spina bifida, meningomyelocele, omphalocele, and other deformities. (28 refs.) - *A. C. Schenker.*

American University of Beirut
Beirut, Lebanon

2288 AICARDI, J.; GOUTIERES, F.; & DE VERBOIS, HODEBOURG. Multicystic encephalomalacia of infants and its relation to abnormal gestation and hydranencephaly. *Journal of the Neurological Sciences*, 15(4):357-373, 1972.

The main features of multicystic encephalomalacia (MCE) are delineated on the basis of 4 cases. The clinical picture is not specific. Onset is generally in the first few days of life. Irritability, apathy, hypotony, or rigidity may be variously observed; cyanosis, apnea, and convulsions may occur. A high protein content was seen in the spinal fluid of 3 of the cases, and in 1 case the gamma globulin was elevated in the CSF. EEG patterns showed no recognizable pattern between sleeping and waking. It is suggested that the association of MCE with twin pregnancy, especially monozygotic, is too frequent to be fortuitous; it was found in 3 of the cases. Evidence for the parabiotic twin syndrome may be adduced from the finding of neonatal anemia in 2 cases; in one case there was no evidence of fetal RBCs or hemoglobin in the mother's blood, which points to the MCE twin having bled into the other. The more frequent use of air studies in chronic encephalopathies is urged. (28 refs.) - *A. C. Schenker.*

Hopital St. Vincent-de-Paul
75 Paris 14, France

2289 **AFIFI, ADEL K.; DER KALOUSTIAN, VAZKEN M.; & MIRE, JOANNE J.** Muscular abnormality in xeroderma pigmentosum: high resolution light-microscopy and electron-microscopic observations. *Journal of the Neurological Sciences,* 17(4):435-442, 1972.

Light- and electron-microscopic findings of a hitherto undescribed muscle lesion, associated both with xeroderma pigmentosum and the De Sanctis-Cacchione syndrome, are described in 3 cases: a 13-year-old boy with the De Sanctis-Cacchione syndrome, and 2 siblings (1½-year-old boy, and a 3-year-old girl) with the simple form of xeroderma pigmentosum. The pathology of muscle in all 3 patients was identical, consisting of massive deposition of glycogen in its free particulate form and of subsarcolemmal aggregates of mitochondria. This type of lesion has not been described before in the De-Sanctis-Cacchione syndrome, which is characterized by MR, dwarfism, gonadal hypoplasia, epilepsy, spastic paraplegia, and other manifestations as well as photosensitivity. It is suggested that the genetic enzymatic defects that are responsible for the cutaneous manifestations may also be responsible for the muscle pathology. (14 refs.) - *A. C. Schenker.*

American University of Beirut
Beirut, Lebanon

2290 **McCARTHY, JAMES W.; & COBLE, LARRY L.** Intracranial hemorrhage and subsequent communicating hydrocephalus in a neonate with classical hemophilia. *Pediatrics,* 51(1):122-124, 1973.

A neonate with classical hemophilia (factor VIII deficiency) who was treated successfully for a subarachnoid hemorrhage developed a secondary communicating hydrocephalus which necessitated a shunting procedure. The Battle's sign without roentgenographic evidence of a skull fracture was probably due to the passage of blood through the open sutures into the postauricular subcutaneous tissue. The case demonstrated that both the acute intracranial hemorrhage and secondary complications could be managed successfully with the use of antihemophilia factor concentrate (Hemophil), administered in amounts of 60 to 100 units every 24 hours in order to maintain a factor VIII level over 50%. (7 refs.) - *B. J. Grylack.*

U.S. Army General Hospital
Fort Gordon, Georgia 30905

2291 **LLOYD, E. L.** Respiratory distress syndrome. *British Medical Journal,* 3(5836):360, 1972. (Letter)

In the light of evidence suggesting that the development of respiratory distress syndrome is due to a pathologic response to the oxygen in the normal atmosphere, alteration of the inspired gases or support of the mechanisms protecting the lungs against the effects of oxygen are possible approaches to the problem. Application of continuous positive pressure to the airway at a sufficiently early stage might allow the oxygen tension in the inspired gases to be reduced below the concentration in the atmosphere. Recent work on the role of the second gas effect on the onset of pulmonary oxygen toxicity indicates an alternative possibility of modifying or preventing the disease by varying the nonoxygen component to a composition less likely to damage the abnormal lungs. Ascorbic acid, pentobarbital and other anesthetic agents, and sympatholytic agents may all be applicable to the lung predisposed to the onset of the respiratory distress syndrome because of

immature antioxidant mechanisms. (13 refs.) - *B. J. Grylack.*

Royal Infirmary
Edinburgh, Scotland

2292 **IBRAHIM, MOHAMED Z. M.** The response of the brain to hypoxia and ischaemia. *Journal of the Neurological Sciences*, 17(3):271-279, 1972.

The effects of several types of hypoxia on rats with unilateral and bilateral carotid ligations were studied in order to elucidate the effects of localized damage to the CNS in humans. The experimental animals were adult male Sprague-Dawley rats who were divided into 4 groups: (1) ischemic, obtained by unilateral carotid ligation; (2) bilateral ischemic; (3) hypoxic–animals exposed to 92.5% nitrogen and 7.5% oxygen, followed by exposure to pure nitrogen; and (4) ischemic-hypoxic. In group 1, a transient reduction in phosphorylase activity and glycogen content was found in the ischemic hemisphere, which returned to normal. Groups 2 and 3 initially showed similar changes in phosphorylase activity which was greatly diminished in both white and gray matter, returning to normal by 6 hr. By about 8 hr an increase in glycogen and in phosphorylase appeared which was more prominent in the hypoxic group in certain sensitive areas. The group 4 animals were examined at varying intervals; by 6-8 hr phosphorylase hyperactivity had occurred and spread throughout the brain. Cytologically, the glycogen and enzymic activities were located mainly within the astrocytes. Several factors may contribute to the vulnerability of the CNS to oxygen or nutritive deprivation. (61 refs.) - *A. C. Schenker.*

American University of Beirut
Beirut, Lebanon

2293 **JOHNSON, A. MYRON.** Alpha$_1$-antitrypsin and infantile respiratory distress. *New England Journal of Medicine*, 288(10):523, 1973. (Letter)

Although Mathis et al. provide evidence for the concept that the deficiency of alpha$_1$-antitrypsin, associated with the idiopathic respiratory distress syndrome (IRDS) in infants, is acquired rather than genetic, the conclusion that there is selective accumulation of alpha$_1$-antitrypsin is more equivocal. The concentrations of fibrinogen and alpha$_1$-antitrypsin in normal newborn plasma are roughly equivalent; if plasma accumulation in the alveolar spaces occurs before plasma alpha$_1$-antitrypsin levels fall, the amounts of both proteins in the fibrin clots would be similar. Infants with IRDS of relatively late onset do have normal serum alpha$_1$-antitrypsin; the others probably do prenatally. It appears reasonable to hypothesize that there is increased intravascular complexing of activated plasmin with alpha$_1$-antitrypsin. The ratio of trypsin inhibitor capacity (as found from accumulated data) to immunochemical alpha$_1$-trypsin levels may be a better diagnostic indicator in IRDS than either level alone. The bound, inactive alpha$_1$-antitrypsin may represent 50-100% of the circulating alpha$_1$-antitrypsin in these infants. (6 refs.) - *A. C. Schenker.*

University of North Carolina School of Medicine
Chapel Hill, North Carolina

2294 **VAN DEN BERGH, R.; & BEULS, E.** Plexectomy in the management of hydrocephalus. *European Neurology*, 8:286-295, 1972.

Plexectomy in the treatment of hydrocephalus is described with the results of such treatment. The surgical procedure comprises an incision at the parieto-occipital transition; after cruciform incision of the galea aponeurotica, a trephining hole is made and the dura mater is cruciformly incised after partial decompression of the lateral ventricle. The lateral ventricle is then opened and an autostatic plastic retractor is inserted. Through the frame of plastic tubes, the plexus chorioideus can be removed. After the first plexectomy, 7 out of 22 cases were definitely stabilized; 13 of the remaining patients were subjected to a second plexectomy, of which 7 had definitive stabilization. The postoperative mortality in 35 plexectomies was 1 case; 3 patients died 17 months, 21 months, and 3 years later, respectively. The principle of plexectomy is based on the concept that the cerebrospinal fluid is produced by the plexus chorioideus; plexectomy may reduce liquor production to an extent permitting balance between production and resorption to be achieved. (17 refs.) - *A. C. Schenker.*

University of Leuven
Leuven, Belgium

2295 **GOLDMAN, ARMOND S.; & GOLDBLUM, RANDALL M.** Familial thymic aplasia—genetic defect or maternal effect. *New England Journal of Medicine*, 288(2):108, 1973. (Letter)

In Steele's description of the first cases of familial aplasia of the thymus and parathyroids, the disorder was attributed to a genetic defect; it is possible that a nongenetic mode of transmission may be implicated. The partial deficiencies of thymic and parathyroid function in the mother of the two affected infants were cited as evidence for maternal transmission either by autosomal or by X-linked dominant inheritance. In this context, a search for antibodies to thymic and parathyroid tissue in the mother of the infants with thymic aplasia may be informative. Although a pathogenic role of such antibodies has not been proven, their placental transfer might influence the development of the specific endocrine organs. (2 refs.) - *A. C. Schenker.*

University of Texas Medical Branch
Galveston, Texas

2296 **DILLARD, ROBERT G.; & *KORONES, SHELDON B.** Lower discharge weight and shortened nursery stay for low-birth-weight infants. *New England Journal of Medicine*, 288(3):131-133, 1973.

The effects of discharging low birthweight infants were compared with those of keeping such infants for a longer time in the nursery, to assess any hazards attributable to early discharge. For one year (September 1970-September 1971), all hospitalized infants who survived the initial 24-48 hr of life and weighed 2,268gm or less at birth were assigned alternatively to A or B discharge groups. To be discharged, Group A infants had to weigh at least 2,000gm and Group B infants had to weigh at least 2,268gm. Additional criteria for infants in both groups were that they be at least 4 days of age, that they have at least 2 consecutive days of weight gain of 15gm/day, and that they be free from acute illness. Of the 410 infants discharged according to criteria, the mean weight at discharge was 2,076gm for Group A and 2,295gm for Group B infants. The mean duration of hospital stay was 18.7 days for Group A and 25.4 days for Group B. Eight of 183 Group A and 10 of 198 Group B infants were rehospitalized in the 4 weeks after discharge. One death occurred in each of the 2 study groups. At one and 4 weeks after discharge, weight gain was not influenced by the weight at discharge. Thus adoption of the lowered discharge weight of low birthweight infants was shortened by 26% without untoward effects. (9 refs.) - *A. C. Schenker.*

*Newborn Center City of Memphis Hospital
5th Floor, Memphis, Tennessee 38103

2297 **MATHIS, RICHARD K.; FREIER, ESTHER F.; HUNT, CARL E.; KRIVIT, WILLIAM; & *SHARP, HARVEY L.** $Alpha_1$-antitrypsin in the respiratory-distress syndrome. *New England Journal of Medicine*, 288(2):59-64, 1973.

The role of $alpha_1$-antitrypsin in the respiratory distress syndrome (RDS) in newborn infants was investigated with respect to trypsin inhibitory capacity, since low levels have been associated with pulmonary diseases in infants and children. Three groups of infants were studied: 34 infants in whom the syndrome developed; sick infants without the syndrome; and normal newborn infants. Of the first group, 12 died and post mortem examination was performed in each. The infants with RDS had lower levels of trypsin inhibitory capacity than those in the other groups. A significant difference existed between all groups ($p<0.005$). Strongly positive fluorescent antibody tagging for $alpha_1$=antitrypsin was localized to the hyaline membrane on histologic examination. Clinical severity correlated with low $alpha_1$-antitrypsin levels; survivors of severe RDS achieved and maintained normal levels of the glycoprotein despite the persistence, in some cases, of severe pulmonary disease. The incorporation of this enzyme inhibitor into the hyaline membrane may account for the low levels in the blood. (44 refs.) - *A. C. Schenker.*

*University of Minnesota Hospitals
Minneapolis, Minnesota 55455

2298 **HELLSTROM, B.** The neurogenic bladder in children with spina bifida: progress and problems. *European Neurology*, 8:303-308, 1972.

Management of the neurogenic bladder in children with spina bifida includes surgical intervention, electrical stimulation, and treatment of urinary tract infections. Most children with myelomen-

ingocele have defective bladder control; in this connection the neurologic level of the lesion determines the efficacy of bladder function. Children demonstrating unilateral involvement of sacral roots were found to have a normal bladder function as well as normal anal sphincter activity. Some cases have a partial detrusor function, at least in the early course, and a recent investigation describes the possible negative effect of a hyperreflexive bladder. Approximately one-third of the children with myelomeningocele are reported to become socially continent after an 8-week training program, involving forced fluid intake and the use of parasympaticomimetic drugs. Electrical stimulation has been effected in experimental dogs, but has not been used in children. Surgical intervention, such as endoresection and Y-V plasty, usually has only a transient effect. Urinary diversion is sometimes effected surgically. Urinary infections in children with spina bifida are difficult to treat; but the value of Gentamicin in bacterial infections has been pointed out. Results of *in vitro* studies of receptor pharmacology may open a new therapeutic approach. (17 refs.) - *A. C. Schenker.*

Karolinska sjukhuset
Stockholm, Sweden

2299 THEILE, URSEL; & MECHTHILD, JENSEN. The Sjogren-Larsson syndrome: a case report. *Humangenetik*, 17:155-159, 1973.

The Sjogren-Larsson syndrome is described in 3 children from one family. The patients showed generalized erythrodermic ichthyosis, associated with significant MR (I.Q. between 32 and 52) and varying degrees of spastic diplegia. Flexural contractures of hips and knees and talipes equinovarus were observed in the 3 cases. In addition, ophthalmologic abnormalities of the fundus were observed. Skin biopsy revealed prolific hyperkeratosis. Consanguinity was probable but was not established. No screening test has yet been devised for the detection of heterozygous carriers of this syndrome, and the carrier shows no clinical or biochemical abnormalities. (4 refs.) - *A. C. Schenker.*

Institut fur Humangenetik der
Universitat Marburg
Federal Republic of Germany

2300 TAUSSIG, LYNN M.; BRAUNSTEIN, GLENN D.; WHITE, BEVERLY J.; & CHRISTIANSEN, RICHARD L. Silver-Russell dwarfism and cystic fibrosis in a twin: endocrine, chromosomal, dermatoglyphic, and craniofacial studies. *American Journal of Diseases of Children*, 125(4):495-503, 1973.

The first description has been given of cystic fibrosis and Silver-Russell dwarfism in the same patient. The subject was a 6-year-old male twin, whose twin sister was normal. Endocrine analysis and chromosome and genetic studies of the patient and his twin yielded no remarkable findings. Dermatoglyphic analysis revealed abnormalities in most family members, the propositus alone manifesting significantly increased atd angles in the range observed in Down's syndrome and predominance of whorl patterns on the feet. In contrast to the normal craniofacial measurements of the twin sister, the patient showed significantly reduced posterior cranial base length and total cranial base, and both the maxilla and mandible were reduced in all measured dimensions, as was facial height. The congenitaily missing teeth and crowding of the dentition observed in the Silver-Russell syndrome by others were evident here. The cause of the syndrome appears to be genetic, and its sporadic occurrence in many cases where there is no history of short stature or other stigmata in relatives and the lack of chromosomal aberrations suggest its frequent association with fresh dominant mutations. (58 refs.) - *B. J. Grylack.*

National Institute of Arthritis,
Metabolism, and Digestive Diseases
Bethesda, Maryland 20014

2301 RIGATTO, HENRIQUE; & BRADY, JUNE P. Periodic breathing and apnea in preterm infants. II. Hypoxia as a primary event. *Pediatrics*, 50(2):219-228, 1972.

Nine healthy preterm infants were studied on 4 or 5 occasions during the first 35 days of life in order to define the relationship between periodic breathing and hypoxia. Respiratory minute volume and alveolar gases were measured with the use of a nosepiece and screen flowmeter, and a comparison was made of ventilation/apnea minute ventilation,

and alveolar and capillary blood gases during periodic breathing induced by hypoxia and during spontaneous periodic breating in room air. The infants were given 21, 19, 17, and 15% O_2 to breathe for 5 minues each and, after a 10-minute interval breathing air, 21, 15, and 21% O_2 also for 5 minutes each. Progressive hypoxia caused the infants to hypoventilate and to breathe periodically more frequently, and it decreased their ventilation/apnea, due primarily to a progressive increase in the apneic interval. One baby subsequently suffered prolonged apnea (longer than 20 seconds), which was preceded by a substantial decrease in minute ventilation and an increase in alveolar carbon dioxide tension. The findings suggest that hypoxia may be a primary event leading to periodic breathing and apnea and indicate that small, carefully controlled increases in inspired O_2 may be warranted to prevent its occurrence. (16 refs.) - *B. J. Grylack.*

University of Rio Grande Do Sul
Porto Alegre, Brazil

2302 **MARGOLIS, CARMI Z.; ORZALESI, MARCELLO M.; & SCHWARTZ, ALLEN D.** Disseminated intravascular coagulation in the respiratory distress syndrome. *American Journal of Diseases of Children*, 125(3):324-326, 1973.

Disseminated intravascular coagulation (DIC) does not contribute significantly to the pathogenesis of idiopathic respiratory distress syndrome (IRDS), nor is it an important contributing factor in the high mortality and frequent intercranial hemorrhages (ICH) found in IRDS. In an experiment specifically planned to determine the role of DIC in IRDS, 11 infants diagnosed as having severe IRDS were studied. Sixteen premature infants with no respiratory distress matched to the experimental Ss for gestational age and birthweight served as controls for determination of normal levels of blood factors V and VIII. Coagulation tests were performed differentially among 4 groups of Ss (A to D). Specific levels of decreased platelet count and decreased factors V and VIII, or decreased fibrinogen and decreased factors V and VIII, were set to define occurrence of DIC. Of the 11 IRDS Ss, only 2 had definite evidence of DIC; one of these died. In 4 other IRDS Ss who died, 3 autopsies were performed showing that all 3 had extensive atelectasis and hyaline membranes, none of the 3 showed evidence of DIC, and 2 of the 3 had ICH. Conflicting reports of the association of DIC with IRDS and ICH are thus resolved by the preponderantly negative associations noted in the test. (18 refs.) - *C. Wares.*

OMERAD, Fee Hall East
Michigan State University
East Lansing, Michigan 48823

2303 **CRUZ-COKE, R.** Birth control, sex-ratio, and anencephaly. *Lancet*, 2(7786):1094-1095, 1972. (Letter)

New demographic data from Chile display trends towards an increasing proportion of primaparous births (31.9% in 1971 vs. 23.3% in 1960) which may be a consequence of massive birth control programs and a decreased birth rate. Associated with these findings is the trend toward the inversion of the sex ratio among stillbirths (0.992 in 1971 vs. 1.241 in 1960) and an increased frequency of anencephaly among live and still births. The findings that a low sex ratio is associated with anencephaly and that the incidence of anencephaly rises with low parity are in agreement with British studies on the epidemiology of anencephaly. Because of the significant alteration of the sex ratio among stillbirths, it is possible that the processes of intrauterine selection and consequently human microevolution may have been changed through the use of birth control programs. (9 refs.) - *V. J. Goldberg.*

Hospital J. J. Aguirre
University of Chile, Santiago

2304 **MACMAHON, BRIAN.** Etiology of congenital defects. *New England Journal of Medicine*, 287(10):514, 1972. (Editorial)

A new factor, ergonovine maleate, has been added to the list of known teratogenic agents. This compound is used as an abortifacient and infants born after such attempts have symptoms resembling the rare 'Poland' anomaly. Many teratogens produce a characteristic syndrome and the mechanism of this specificity is of interest. - *V. J. Goldberg.*

2305 **BROOK, D. J. H.; & SCRIMGEOUR, J. B.** Early prenatal diagnosis of anencephaly. *Lancet*, 2(7789):1252-1253, 1972. (Letter)

Measurement of the levels of amniotic fluid alpha fetoprotein (AFP) may be used in the prenatal

diagnosis of anencephaly. Amniotic fluid obtained at 18 wks of a pregnancy which resulted in an anencephalic birth had an AFP concentration of 214 micrograms/ml vs 14.9 micrograms/ml in 15 control amniotic fluids of the same gestational age. The AFP levels in anencephalic fluid were high when expressed per mg protein or per mg albumin. The difference between AFP levels in anencephalic and control amniotic fluids at 18 wks was much greater than at 25 or 35 wks. (1 ref.) - *V. J. Goldberg.*

Western General Hospital
Edinburgh 4, Scotland

2306 **KROVETZ, L. JEROME; & ROWE, RICHARD D.** Patent ductus, prematurity and pulmonary disease. *New England Journal of Medicine*, 287(10):513-514, 1972. (Editorial)

The neonate who presents with patent ductus arteriosus frequently is premature, has RDS or post-rubella syndrome, and has a poor prognosis. Kitterman et al. performed surgery on 4 of 12 premature patent ductus neonates without RDS, on 2 of 9 who were recovering from RDS, and on 1 of 2 with chronic lung disease. The necessity for surgery among these groups is debatable. Surgery was performed on 3 of 6 with severe RDS, and only one survived. The factors contributing to the heart failure and RDS in these infants need to be investigated. (7 refs.) - *V. J. Goldberg.*

2307 **ZAMENHOF, S.; & HOLZMAN, G. B.** Study of correlations between neonatal head circumferences, placental parameters and neonatal body weights. *Obstetrics and Gynecology*, 41(6):855-859, 1973.

The search for factors that determine prenatal brain development in normal term infants led to the study of correlations between neonatal parameters of the brain, such as head circumferences and placental and body weights. The Ss were 55 male and 36 female infants of normal appearance and weights on delivery of between 2,700 and 4,000 gm. Placentas within 6 hours after delivery were cleaned, blotted, and weighed; fronto-occipital head circumferences were measured between 24 and 48 hours after delivery. Placental DNA and protein were also determined. Highly significant correlations were found between placental and neonatal body weight, neonatal head circumference and body weight, and between placental parameters: weight vs DNA, weight vs protein, and DNA vs protein. The factors which determine the size of placenta are largely unknown, but the functions involved, which may be conditioned by size of placenta, are extremely important to the developing brain: supply of nutrients and oxygen, removal of waste material, and production of placental hormones. (30 refs.) - *A. C. Schenker.*

UCLA School of Medicine
Los Angeles, California 90024

2308 **SADOVSKY, E.; & YAFFE, H.** Daily fetal movement recording and fetal prognosis. *Obstetrics and Gynecology*, 41(6):845-850, 1973.

In order to decrease the rate of intrauterine fetal death, the value of a Daily Fetal Movements Record (DFMR) is demonstrated in cases of high-risk pregnancy in which placental insufficiency is suspected. Fetal movements, usually felt by the mother in the fifth month of pregnancy, are significantly reduced in cases of placental insufficiency or cease completely. In the cases cited the women were instructed to record each fetal movement from 8 AM to 8 PM; the sum of these for a 12-hr period comprised the DFMR. The first 2 cases revealed that prior to intrauterine fetal death the DFMR decreased to zero, although fetal heartbeats remained normal; a cesarean section during this period could have prevented fetal loss. Such operations were conducted in cases 3, 4, and 5, resulting in the births of living infants. In cases 6 and 7 the patients had severe placental insufficiency, but with the aid of DFMR it was possible to await improved viability of the fetus. The DFMR movements should be recorded in ambulatory patients for 3 hr daily at 1-hour intervals and this record followed for prognostic purposes. (5 refs.) - *A. C. Schenker.*

Mayer De Rothschild Hadassa University Hospital
Jerusalem, Israel

2309 **HAMILTON, LEWIS A., JR.; SZUJEWSKI, PETER F.; & PATEL, MINU K.** Combined sonographic and biochemical estimation of fetal maturity in high-risk pregnancy. *Obstetrics and Gynecology*, 41(6):837-844, 1973.

A model is presented for estimation of fetal age in high-risk patients, using as criteria amniotic fluid creatinine, fetal biparietal diameter, and estimated

fetal weight. Records of 126 cases with data for amniotic fluid studies and fetal cephalometry before delivery were examined. The admitting resident estimated fetal weight by abdominal palpation, and this together with data for fetal cephalometry and amniotic fluid creatinine were key-punched onto individual computer cards for analysis. The computer analysis consisted of the adaptation of a biologic model and the development of its appropriate constant and exponents. A fetal maturity table constructed by the use of the maturity equation was validated by further testing (54 cases). The results strongly supported the method of estimating gestational age in the latter weeks of pregnancy (34-41 weeks), particularly with regard to high-risk patients. (19 refs.) - *A. C. Schenker.*

The Abraham Lincoln School of Medicine
Chicago, Illinois 60612

2310 **MARIONA, FEDERICO G.** Carbohydrate metabolism in the fetal brain during experimental hypoxia. *Obstetrics and Gynecology*, 41(4):640, 1973. (Abstract)

Experimental creation of fetal hypoxia is described for the study of biochemical changes in the fetal blood, brain tissue, and heart. A mathematical interrelationship was noted between lactic acid content in the fetal blood and alterations in the fetal heart rate (bradycardia) as the period of hypoxia was increased. There was no mathematical correlation between lactin acid content of brain tissue and the fetal heart rate changes. A parallel correlation was demonstrated between lactic acid levels in the fetal blood and brain tissue. The accumulation of acid catabolites may be due to an anaerobic glucose metabolism in the fetal brain and produces the changes in heart rate during intrauterine anoxic or hypoxic distress. - *A. C. Schenker.*

Wayne State University School of Medicine
Detroit, Michigan

2311 **AVERY, MARY ELLEN.** Commentary: Prevention of hyaline membrane disease. *Pediatrics*, 50(4):513-514, 1972.

The description of efforts to extend to premature infants the results of studies in animals of hyaline membrane disease in 2 papers (Liggins and Howie, and Baden, et al.) is commented upon. Both papers include the evidence and reasoning for the use of glucocorticoids to accelerate lung maturation in order to prevent the consequences of surfactant deficiency. The significance of the observations in animals lies in the area of understanding the mechanism of hormonal action, for which the fetal lung now becomes an important model. The way in which this research illustrates the value of encouraging interdisciplinary investigation and exchange of ideas between individuals with related interests is pointed out. (12 refs.) - *A. C. Schenker.*

Montreal Children's Hospital
Montreal 108, Quebec, Canada

2312 **HOLM, WILLIAM W.** The respiratory distress syndrome: bronchial arteries and catecholamines. *Pediatrics*, 50(6):973, 1972. (Letter)

Hormones beneficial *in utero* may possibly be detrimental to the newborn infant, who is physiologically immature and prone to the respiratory distress syndrome (RDS). High-pressure, low-volume bronchial artery flow competes with low-pressure, high-volume pulmonary artery flow for alveolar perfusion and effective pulmonary artery flow ceases. Stasis produces edema, which exceeds the clearance capacity of the pulmonary lymphatics. Shunting occurs at the ductus arteriosus. Although the ductus arteriosus receives innervation from the vagus and is constricted by acetylcholine, experimental RDS has been produced by overwhelming cholinesterase blockade, leaving the role of the parasympathetic system to be further delineated. (16 refs.) - *A. C. Schenker.*

491 Allendale Rd.
King of Prussia, Pennsylvania 19406

2313 **WOODRUM, DAVID E.; OLIVER, T. K., JR.; & HODSON, W. ALAN.** The effect of prematurity and hyaline membrane disease on oxygen exchange in the lung. *Pediatrics*, 50(3):380-386, 1972.

The magnitude of the alveolar-arterial oxygen gradient ($AaDO_2$) was investigated in early gestation infants both with and without hyaline membrane disease (HMD) and its relationship to gestational and postnatal age was examined. Two groups of 17 infants were studied throughout the first 4 days of life. Infants in Group 1 had no clinical evidence of respiratory distress and were eucapnic; they had no radiological evidence of pulmonary disease. The mean gestational age was 29 weeks; 8 of these infants died during the first 2

weeks of life. There was no evidence of lung disease at postmortem. No infant in this group received ventilatory support. The group 2 infants had clinical and radiological evidence of HMD and were comparable to group 1 in gestational age. Sixteen of these infants died during the first 7 days of life; 15 of these infants were supported with mechanical ventilation. The mean $AaDO_2$ for the group 1 infants during the first 24 hr was 358mm Hg; that of group 2 infants 557mm Hg. The mean $AaDO_2$ for the infants in group 1 was significantly correlated with gestational age, but there was no such correlation for group 2 infants. The size of $AaDO_2$ in the infants without HMD may be a function of lung development; the right to left shunt probably occurs within the lung itself. (36 refs.) - *A. C. Schenker.*

Department of Pediatrics
University of Washington School of Medicine
Seattle, Washington 98105

2314 **SHURTLEFF, DAVID B.; FOLTZ, ELDON L.; & LOESER, JOHN D.** Hydrocephalus: a definition of its progression and relationship to intellectual function, diagnosis, and complications. *American Journal of Diseases of Children*, 125(5):688-693, 1973.

The relationship between preoperative brain mass and intellectual function 2 or more years after the original operation on hydrocephalus is discussed. The evaluation applies to 222 patients; preoperative evaluations included complete neurological assessment, studies for known biochemical and systemic infectious disorders, and gas-contrast brain roentgenography. The amount of preoperative ventriculomegaly was measured by head size and cerebral mantle width; occipitofrontal circumference (OFC) and ventriculoskull distance (VSD) were used as a measure of brain mass. The patients appeared to fall into macrocephalic or normocephalic infants with less than 0.5cm of frontal cerebral mantle with subsequent MR, or a group with 1.0cm or more of cerebral mantle. In the group with thicker cerebral mantles, those with a small head have a smaller cerebral mass and poor intellectual development. Children with less than 60% of normal brain mass prior to operation were found to be significantly retarded. It is stressed that both OFC and VSD must be obtained for prediction of intellectual performance. (25 refs.) - *A. C. Schenker.*

University of Washington School of Medicine
Seattle, Washington

2315 **EDWARDS, NEIL K.; ATHERTON, HARRY D.; *PERLSTEIN, PAUL H.; & SUTHERLAND, JAMES M.** Phantom breathing in monitored infants. *American Journal of Diseases of Children*, 125(5):684-685, 1973.

Outlet voltage fluctuations which were considered capable of influencing the function of an apnea monitor in the treatment of infants were discovered in a nursery, and a report is presented to alert nursery personnel to this possibility. Five monitors were connected to a simulated apneic patient and test results noted; the line voltage fluctuated between 103 and 114 v. At 120 v, and when the voltage was initially lowered, apnea was correctly indicated, until a critical voltage (upper false respiration threshold) was reached. As the voltage was lowered from this level, breathing was falsely indicated on the dial and the auditory and visual alarm ceased. False respirations (phantom breathing) were continually indicated until the lower false respiration threshold was reached. It is suggested that the electronic monitoring devices be evaluated for fluctuations in the power system, and that manufacturers of medical electronic equipment take adequate precautions in designing the systems. - *A. C. Schenker.*

Children's Hospital Research Foundation
Cincinnati, Ohio 45229

2316 **BALLARD, ROBERTA; KRAYBILL, ERNEST N.; HERNANDEZ, JACINTO; RENFIELD, MARILYN L.; & *BLANKENSHIP, WILLARD J.** Idiopathic respiratory distress syndrome: treatment with continuous negative-pressure ventilation. *American Journal of Diseases of Children*, 125(5):676-681, 1973.

The management of idiopathic respiratory distress syndrome (IRDS) by means of continuous negative pressure ventilation (CNPV) is described in 79 infants. Of these, 66 (84%) survived; all of these survivors sustained rises in their PO_2 of more than 20mm Hg within 2 hr following the institution of CNPV. The 2 major disadvantages of CNPV are: gastric dilation, which necessitates continuous suction with an indwelling catheter and postpones

adequate calorie intake; and the relative inaccessibility of the infant's body to examination and manipulation. There were 3 infants who had some residual pulmonary findings at the time of discharge from the nursery; 2 of these were asymptomatic but had radiographic changes. The infants with residual pulmonary findings had CNPV instituted earlier and required longer exposure to an enriched oxygen environment than those with normal chest roentgenograms. None of the infants developed clinical cardiac failure or required ligation of the ductus. (31 refs.) - *A. C. Schenker.*

*Sacramento Medical Center
University of California at Davis
Sacramento, California 95817

2317 **DOOLITTLE, WALTER M.; OHMART, DAVID; & EGAN, EDMUND A.** Congenital bilateral pleural effusions: a cause for respiratory failure in the newborn. *American Journal of Diseases of Children*, 125(3):435-437, 1973.

The successful management of an infant with bilateral, massive, noninfectious, congenital pleural effusions by repeated thoracenteses with low pressure suction is described. The pleural fluid has a protein content of 2.5-3.0gm/100ml; total fats of 150-200mg/100ml; triglycerides of 40-60mg/100ml; cholesterol of 52-110mg/100ml; and a WBC of 4000-5000, all lymphocytes. The analysis was consistent with chyle in the absence of long chain fat feedings. The normal pulmonary arteriogram and the rapid and complete resolution of the effusions and respiratory embarrassment, once adequate drainage was maintained, indicate that the effusion alone was the cause of the respiratory insufficiency. (7 refs.) - *A. C. Schenker.*

Madigan General Hospital
Tacoma, Washington 98431

2318 **PASHAYAN, HERMINE; PRUZANSKY, SAMUEL; & PUTTERMAN, ALLEN.** A family with blepharo-naso-facial malformations. *American Journal of Diseases of Children*, 125(3):389-393, 1973.

A congenital dysmorphic syndrome, characterized by telecanthus, lateral displacement of the puncta from the inner canthi, bulky nose, mask-like facies, torsion dystonia, and MR is described in 4 members of one family. The affected members showed normal chromosomes and normal urine amino acid chromatography, and the associated dysmorphic characteristics appeared to be unique. This syndrome shows variable expressions between individuals of the same family. The pedigree is compatible with Mendelian dominant inheritance, either autosomal or X-linked. (14 refs.) - *A. C. Schenker.*

Center for Craniofacial Anomalies
University of Illinois
Chicago, Illinois 60680

2319 **BOYNTON, RAGNA C.; & *MORGAN, BEVERLY C.** Cerebral arteriovenous fistula with possible hereditary telangiectasia. *American Journal of Diseases of Children*, 125(1):99-101, 1973.

An infant with a large cerebral arteriovenous (AV) fistula, born to a family with known hemorrhagic telangiectasia (HHT), is described. Although such association of AV fistulas with familial HHT is unique, such manifestation is plausible in this case. The additional occurrence of a symptomatic AV malformation of the spinal cord in the patient's father, who had known HHT, may indicate a propensity for major manifestations of the disease to occur in the central nervous system in this particular family. Reports in the literature are reviewed in reference to hereditary hemorrhagic telangiectasia, pathological findings, symptoms, and central nervous system involvement. (23 refs.) - *A. C. Schenker.*

*University of Washington School of Medicine
Seattle, Washington 98195

2320 **EKELUND, H.; & FINNSTROM, O.** Fibrin degradation in hypoxic full-term neonates. *British Medical Journal*, 1(5795):312-313, 1972. (Letter)

The interpretation of the findings by Chadd that a significant correlation was found between a low Apgar score and raised levels of fibrin degradation products (F.D.P.) (≤ 5) is considered faulty. A study is cited in 154 infants demonstrating that there is indeed a positive correlation between a low Apgar score and raised levels of F.D.P. However, Dr. Apgar has pointed out that the score at 1 min does not reflect oxygenation itself.

Furthermore, biochemical confirmation of hypoxia obtained by capillary blood gas determinations is inappropriate and must be performed on arterial blood. A one-min score and capillary oxygen tension assays do not warrant a suggestion of a causal relationship between hypoxia and raised levels of F.D.P. In the study cited, moreover, only levels of <10 microgm/ml were accepted as being of pathological significance. (5 refs.) - *A. C. Schenker.*

General Hospital
Malmo, Sweden

2321 CHADD, M.A.; ELWOOD, P. C.; GRAY, O. P.; & MUXWORTHY, S. M. Hypoxic newborn infants. *British Medical Journal*, 1(5795):309, 1972. (Letter)

In response to comments by Wigglesworth regarding the article in which an association was noted between asphyxia at birth and blood coagulation changes in the full-term newborn infant, the conclusion that the hypoxic babies had disseminated intravascular coagulation is reiterated. Evidence for this includes lowered platelet counts, raised levels of fibrin degradation products, and prolonged thrombin clotting times. It is therefore believed that such babies are at serious risk of spontaneous hemorrhage, as the process of intravascular coagulation is accompanied by a reduction in certain coagulation factors. It is also relevant that antenatal complications had occurred with 46% of the anoxic infants. (3 refs.) - *A. C. Schenker.*

Welsh National School of Medicine
Cardiff, Wales

2322 GHADIMI, H.; ARULANANTHAM, K.; & DESAI, L. Unitary concept for prevention and treatment of respiratory-distress syndrome. *Lancet*, 2(7821):126-128, 1973.

A deficiency of surfactant is the major factor in the vicious circle of the respiratory distress syndrome, in which reduced compliance of alveoli on respiration leads to atelectasis, hypoxia, carbon dioxide retention, acidosis, vasoconstriction, hypoperfusion of the lungs, transudation, and further inhibition of surfactant formation. Preoccupation with anoxia and the need for oxygen therapy may have diverted attention from substrate deficiency and starvation. Study of the arteriovenous differences in aminoacid concentration of blood taken from the forearm indicated that premature infants may receive as little as 80mg of aminoacid from skeletal muscle, a figure far below the recommended daily protein allowance of 4,500mg. In view of the postnatal scarcity of resources, only corticosteroids administered prenatally could possibly enhance surfactant formation, with the fetus having access to the maternal sources of substrate. Preliminary experience with total parenteral nutrition in infants with respiratory distress syndrome, however, has shown a favorable response and significant modification of the disease course when an adequate supply of carbohydrate and proper solutions of aminoacids, primarily those which provide substrate for branched-chain fatty acid, are administered. (21 refs.) - *B. J. Grylack.*

Methodist Hospital
Brooklyn, New York 11215

2323 KOZŁOWSKI, K.; RAFINSKI, T.; & KUCHARSKA, K. Metaphyseal and epiphyseal dysplasia with unusual facies and cataract. *American Journal of Diseases of Children*, 125(4):533-556, 1973.

A 10-year-old girl presenting with low-birthweight dwarfism, retarded mental and physical development, bilateral cataracts, peculiar facies, bat ears, scanty subcutaneous tissue, knee deformities, and the radiographic changes of metaphyseal and epiphyseal bone dysplasia may be suffering from an unidentified syndrome. Her abnormalities are not fully consistent with the known premature senility syndromes or the meta-epiphyseal and epimetaphyseal dysplasias, and her condition probably represents a separate progeroid syndrome. (15 refs.) - *B. J. Grylack.*

Royal Alexandra Hospital for Children
Camperdown 2050, NSW, Australia

2324 CYVIN, K. B.; WEIDEMANN, J.; & BATHEN, J. Lowe's syndrome. *Acta Paediatrica Scandinavica*, 62(3):309-312, 1973.

A male child and a female born to the same mother but allegedly of a different father manifested the typical findings of the oculuo-cerebro-renal syndrome of Lowe. Both had severe renal damage resulting in a fatal outcome at the age of 3 to 4 months. X-linked recessive and sex-linked

dominant inheritance were considered unlikely in this family, since the girl was severely affected, and the fact that the mother was unaffected made autosomal dominant inheritance unlikely. Autosomal recessive inheritance, requiring that both fathers were heterozygotes, would be possible only if the same man was in fact the father of both children or if the 2 fathers were related. (14 refs.) - *B. J. Grylack.*

Sentralsykehuset
Trondheim, Norway

2325 **LEEK, A. E.; RUOSS, C. F.; KITAU, M. J.; & CHARD, T.** Raised α-fetoprotein in maternal serum with anencephalic pregnancy. *Lancet*, 2(7825):385, 1973. (Letter)

Three cases of anencephaly were studied, the levels of α-fetoprotein in maternal serum and/or amniotic fluid being estimated by radioimmunoassay. The levels in amniotic fluid were increased in the 2 cases for which material was available. Maternal serum levels were also elevated in 2 of 3 cases, although the third case showed normal maternal levels in association with high amniotic fluid concentration. The data suggest that the increased levels in amniotic fluid may be reflected in maternal blood. (5 refs.) - *B. J. Grylack.*

St. Bartholomew's Hospital
London EC1A 7BE, England

2326 **PANDYA, S. K.** Neonatal hydrocephalus treated by compressive head wrapping. *Lancet*, 2(7824):334, 1973. (Letter)

Previously described patients with normal or only slightly elevated intraventricular pressure who were treated by compressive headwrapping might have proved to have "compensated" or arrested hydrocephalus, in any case. Aspiration of cerebrospinal fluid from hydrocephalic patients has been associated in the past with the difficulty of regulating an elastic bandage in such a way as to exert sufficient pressure to prevent expansion without causing undue compression. (2 refs.) - *B. J. Grylack.*

Department of Neurosurgery
K. E. M. Hospital
Parel, Bombay 12, India

2327 **WETTRELL, G.; SVENNINGSEN, N. W.; NORDENFELT, E.; & LINDHOLM, KARIN.** Clinical manifestations of Letterer-Siwe disease in the neonatal period. *Acta Paediatrica Scandinavica*, 62(3):321-323, 1973.

The clinical course of an infant born with Letterer-Siwe disease was dominated by several elevated, ulcerated nodules and a disseminated bluish-red maculopapular rash noted at birth. During the first week of life the maculopapular skin lesions remained almost stationary. During the following days bacteriologic cultures from the skin lesions showed plasmacoagulating *Staphylococcus aureus*. Fine-needle biopsy from an inguinal lymph node obtained on the first day of life revealed a cytologic picture compatible with reticuloendotheliosis. Treatment was planned with antimetabolites but not carried out due to a rapid decline in the infant's condition culminating in death on the eighteenth day of life. Biopsy of skin lesions and fine-needle aspiration of existing lymph nodes should be performed without delay in these cases, since early treatment may induce remission. (13 refs.) - *B. J. Grylack.*

University Hospital
S-221 85 Lund, Sweden

2328 **STEIN, S. M.; & MONAGHAN, J. M.** Prediction of respiratory distress syndrome. *Lancet*, 2(7825):378, 1973. (Letter)

Great care must be taken in interpreting lecithin/sphingomyelin ratios performed on bloodstained samples. Addition of 20μl of whole blood to 3ml of amniotic fluid caused a reduction in a lecithin/sphingomyelin ratio of 4.0/1.0 to 3.1/1.0, and the ratio was halved to 2.0/1.0 when 80μl of whole blood was added to the 3ml of amniotic fluid. The range of apparent lecithin/sphingomyelin ratios obtained in maternal and fetal blood varies from 0.6/1.0 to 1.7/1.0. Thus, the high ratios in amniotic fluid will be depressed by an amount dependent upon the extent of contamination. Interpretation of the "shake" test may also be affected by contamination of the liquor with blood. (2 refs.) - *B. J. Grylack.*

Western General Hospital
Edinburgh EH4 2XU, Scotland

2329 **LIU, DAVID T. Y.** Phosphodiesterase inhibition and respiratory-distress syndrome. *Lancet*, 2(7825):378-379, 1973. (Letter)

In 2 independent observations, the favorable outcome of premature infants has been reported following β-sympathomimetic administration to the mother, and premature infants with an average weight of 1,866.5g have been delivered in good health or with subsequent successful recovery from transient respiratory distress despite attempts to delay premature labor by phosphodiesterase inhibition with a methylxanthine. Fetal tachycardia was noted in both studies, and intracellular 3′5′-adenosine monophosphate increased after β-adrenergic stimulation and after phosphodiesterase inhibition. (6 refs.) - *B. J. Grylack.*

Royal Sussex County Hospital
Eastern Road
Brighton, Sussex, England

2330 **SANDLER, BERNARD.** Anencephaly and ovulation stimulation. *Lancet*, 2(7825):379, 1973. (Letter)

Anencephaly occurred with ovulation stimulation in the case of a 25-year-old woman who did not ovulate adequately, whose husband was sterile, and who received clomiphene in order to allow her to conceive. She was hospitalized subsequently with very marked hydramnios, and an X-ray confirmed that the baby was an anencephalic. The patient must have been under the influence of clomiphene when conception took place, although the possibility that an aged ovum or an aged sperm may have been involved could not be excluded. (1 ref.) - *B. J. Grylack.*

13 St. John Street
Manchester M3 4DQ, England

2331 Genetic causes of mental subnormality. *Lancet*, 2(7820):83-84, 1973. (Editorial)

Some causes of MR are reviewed, including the known genetic and metabolic etiologies. It is known that an abnormal number of autosomes, if compatible with survival, will result in severe MR; the best known example is Down's syndrome. Aneuploidy of the sex chromosomes carries an increased risk of a higher grade of subnormality and may include antisocial behavior. Several genetically determined disorders of protein, lipid, pigment, and mineral metabolism result in MR, as do many congenital malformations of the central nervous system, based on a mendelian form of inheritance. An X-linked mode of inheritance for some types of MR has been discovered. Families with disorders of aminoacid metabolism have been investigated with findings that should stimulate further research. Most patients with MR still cannot be assigned to a precise diagnostic category. (4 refs.) - *A. C. Schenker.*

2332 **GENT, W. L. G.** Lactic acidosis. *Lancet*, 2(7822):198-199, 1973. (Letter)

The assertion that the production of lactate from pyruvate ions is possibly homeostatic is based on faulty argument. At the physiological pH, the fractions of the total acids present as unionized pyruvic and lactic acids are 9.1×10^{-6} and 2.1×10^{-1}, respectively, calculated as effective pK. While it is true that there would be 23 times more lactic than pyruvic acid molecules, the diminution of hydrogen ion would be only 0.2 micromole/mmole of pyruvic acid transformed. Thus, in a lactic acidotic condition the extra hydrogen load imposed on the blood would be reduced by only about 0.02%, an effect which is too small to be called homeostatic. - *A. C. Schenker.*

Guy's Hospital Medical School
London SE1 9RT, England

2333 **KERO, PENTTI; HIRVONEN, TOIVO; & VALIMAKI, ILKKA.** Prenatal and postnatal isoxsuprine and respiratory-distress syndrome. *Lancet*, 2(7822):198, 1973. (Letter)

The effects of isoxsuprine treatment on the fetus in premature labor were studied. Of 26 premature infants whose mothers were treated with isoxsuprine during labor, only 2 died, both of a congenital malformation. Slight respiratory difficulties were found in 2, but none had any typical respiratory distress syndrome (RDS). Because of respiratory maladaptation and prematurity per se, 3 infants were on a positive-pressure respirator. In another study of 12 labors, i.v. isoxsuprine was given (80-160mg per 1-2 days) up to the end of labor. All these infants were born without RDS or peripheral edema. Isoxsuprine is a β-sympathicostimulant with a possible mild α-inhibitory effect and a direct papaverine-like effect. It seems jus-

tifiable to use this agent prenatally in small premature infants. (4 refs.) - *A. C. Schenker.*

University of Turku
Turku, Finland

2334 **SELLER, MARY J.; COLTART, T. M.; CAMPBELL, STUART; & SINGER, J. D.** Early termination of anencephalic pregnancy after detection by raised alpha-fetoprotein levels. *Lancet,* 2(7820):73, 1973.

Transabdominal amniocentesis was performed on at-risk women at 17-18 weeks of gestation in response to those seeking genetic advice who had had an anencephalic child previously. The amniotic fluid of one of these patients had a very high α-fetoprotein (AFP) of 380 microgm/ml. This woman had given birth to a stillborn anencephalic child with spina bifida 17 months previously. On subsequent ultrasound examination, no fetal head could be discerned. The pregnancy was terminated by instillation of 25mg of prostaglandin F_2a into the amniotic cavity at the twentieth week of gestation, and a fetus with anencephaly was delivered. It is submitted that AFP coupled with ultrasound measurements may be used for diagnostic purposes in such cases. (5 refs.) - *A. C. Schenker.*

Guy's Hospital Medical School
London, England

2335 **SEVER, LOWELL E.** Parity, potatoes, and spina bifida. *Lancet,* 2(7821):161, 1973. (Letter)

The suggestion by Renwick that the mother of a child with a neural tube defect conceives her first child before she leaves her parents' home, where she is exposed during the pregnancy to a potato-associated teratogen, thus increasing the risk of a child with such defect, is contradicted by the results of an epidemiological study. In this study of spina bifida, data were collected from case mothers and controls as to whether or not they were living with their parental family at the time of their marriage. In all comparisons the affected child was first-born. Of the case mothers with sisters, 8 (50%) were living with their parental family at the time of their marriage and 8 were not. For their sisters, 10 (62%) were living with their parental family while 6 (38%) were not. Of the case mothers without sisters, 10 were living with their parental family and 10 were not. For the matched controls, 7 (35%) were living with their parental family and 13 were not. Neither of these differences is statistically significant. The primogeniture effect in neural-tube defects is probably related to intrinsic biological characteristics of the mother and not to exposure to an environmental teratogen. (1 ref.) - *A. C. Schenker.*

University of Washington
Seattle, Washington 98105

2336 **FISHER, P. M.; SUTHERLAND, H. W.; DINWIDDIE, R.; & RUSSELL, G.** Shake test on amniotic fluid and the respiratory distress syndrome. *British Medical Journal,* 2(5863):423, 1973. (Letter)

Commenting on Bhagwanani's findings and others, it is confirmed that a negative shake test on amniotic fluid is of poor predictive value for respiratory distress syndrome (RDS), whereas a positive zone result reflects the absence of RDS risk. From a study of 86 shake tests within 36 hr of delivery, 58 gave positive zone results, 17 gave intermediate zone results, and 11 gave negative zone results. Of the 86, only one neonate (34 weeks' gestation) with a negative shake test and lecithin concentration of 3.88mg/100ml showed any evidence of RDS, but this was attributed to maternal chlormethiazole therapy. Of the 11 cases with negative zone results, excessive volumes of amniotic fluid, in 5 cases, may have influenced the interpretation of the shake test results. Pulmonary hypoplasia, associated with a negative shake test, as described by Bhagwanani, was also found in a fresh stillbirth with multiple congenital abnormalities. It is suggested that the critical lecithin concentration of 3.5mg/100ml suggested by Bhaganani may be too low. (5 refs.) - *A. C. Schenker.*

University of Aberdeen
United Kingdom

2337 **CRUZ-COKE, R.** Anencephaly and potatoes in Chile. *Lancet,* 1(7797):269-270, 1973. (Letter)

Preliminary data are reported, in connection with Renwick's hypothesis that blighted potatoes are

related to the increase of anencephaly in Chile. The potato crops, yields, kg/head, and anencephaly per 1,000 births are tabulated for the years 1959 through 1971. Although it is tempting to correlate potato production and frequency of anencephaly, the recent decrease in production may be explained by a long drought and massive collectivization affecting nearly 50% of the arable land. The anencephaly rate has increased from .13/1,000 in 1959 to .31/1,000 in 1971, in spite of the introduction of potato-blight-resistant potatoes, covering these years, and the in-between interval. (4 refs.) - *A. C. Schenker.*

Hospital J. Aguirre
University of Chile
Santiago, Chile

2338 **SMITH, C.; WATT, MURIEL; BOYD, A. E. W.; & HOLMES, J. C.** Anencephaly, spina bifida, and potato blight in the Edinburgh area. *Lancet,* 1(7797):269, 1973. (Letter)

Data from the Edinburgh area dealing with blight in the potato crop and conception in the same crop year are submitted as evidence of a lack of association between the severity of potato blight and the frequency of anencephaly and spina bifida claimed by some investigators. Records on all stillbirths and deaths under 28 days were available for the period 1954-1971 from the birth registers of the largest maternity hospital in the area, as were details of the reported month of conception. Blight scores for the potato crop were derived from assessment of progress of the disease on potato haulm. Years with high blight scores showed no tendency to have a high number of cases of anencephaly and spina bifida. The data did show highly significant monthly differences in the number of cases; conceptions of cases were markedly elevated in May and August and were low in February. Thus, the association between conception and blight showed no correlation to the frequency of cases of anencephaly and spina bifida. (5 refs.) - *A. C. Schenker.*

Western General Hospital
Edinburgh EH4 2HU, Scotland

2339 **HICKEY, RICHARD J.; CLELLAND, RICHARD C.; & HARNER, EVELYN B.** Smoking, birth-weight, development, and pollution. *Lancet,* 1(7797):270, 1973. (Letter)

The concept that smoking during pregnancy may be harmful to the fetus because of its association with intrauterine growth retardation and increased perinatal death rates is criticized on the basis that the harmful effects to the fetus are due to the smoker, rather than the smoking per se. Quoting Yerushalmy, this is explained by the fact that a certain type of woman smokes in response to some inner need and that the association with the harmful effects to the fetus, as stated by Hardy and Mellits, cannot validate an hypothesis. The greater concordance in smoking behavior among monozygotic than among dizygotic twins is compatible with the constitutional hypothesis but discouraging to the smoking-causality hypothesis. The constitutional hypothesis asserts that smoking behavior of women and the birthweights of their children are influenced by a common cause: the individual genotype. Smoking behavior may be, for some people, a symptom or effect of an underlying limitation of physiological bioenergetics; this applies to glucose metabolism or catecholamine release, following nicotine. (31 refs.) - *A. C. Schenker.*

The Wharton School
University of Pennsylvania
Philadelphia, Pennsylvania 19174

2340 **OPITZ, JOHN M.** Pregnancy in woman with meningomyelocele. *Lancet,* 1(7799):368, 1973. (Letter)

In response to a letter by Fujimoto, the case of a 35-year-old woman with a small lumbar meningomyelocele and mild paresis of the lower extremities who has become pregnant for the third time is described; her first child was stillborn with meningomyelocele, hydrocephalus, and a bilateral club-foot deformity; and a therapeutic abortion was performed 10 years later when she became pregnant again. When genetic counseling was applied for, the couple were told that the risk of fetal defect was about the same as for the case of normal parents who had had two affected children, 1 in 7. The risk figure was unacceptable to the woman, and a therapeutic abortion was performed. This fetus was grossly entirely normal; histological studies were not performed. - *A. C. Schenker.*

University of Wisconsin
Center for Health Sciences and Medical School
Madison, Wisconsin 53706

2341 **SEPPALA, MARKKU; & RUOSLAHTI, ERKKI.** Alpha-fetoprotein in antenatal diagnosis. *Lancet,* 1(7795):155, 1973. (Letter)

A comparison of α-fetoprotein (AFP) concentrations with those reported by Brock and Sutcliffe in fetal anencephaly and spina bifida shows their results to be much higher than those found in normal amniotic fluid reported below. AFP concentrations were determined by radioimmunoassay in both amniotic fluid and maternal serum; the highest serum AFP levels were found to be about 500ng/ml during the mid-third trimester. In amniotic fluid, the highest AFP levels were 26,000ng/ml at 14-15 weeks of gestation. AFP concentrations in normal pregnancies decreased subsequently: mean concentration at 35-36 weeks, 316; 37-38 weeks, 164; 39-40 weeks, 115; and 41-42 weeks, 87 (ng/ml). In the control material of Brock and Sutcliffe, concentrations of about 6,000ng/ml were found in week 39. The conflicting results can only be explained by the different standards used. Some results in abnormal pregnancies are cited. It was found, in contrast to Brock and Sutcliffe, that AFP concentrations in amniotic fluid can be affected by fetal distress. It would be important to know if the high "normal" results reported by these investigators were from Rh-immunized pregnancies, and whether the anencephalic fetuses were distressed or dead at the time samples were taken. (8 refs.) - *A. C. Schenker.*

Department II of Obstetrics and Gynecology
University Central Hospital
SF-00290 Helsinki 29, Finland

2342 **MILLS, WILFRID.** Pregnancy and meningomyelocele. *Lancet,* 1(7796):208, 1973. (Letter)

A pregnancy in a woman with a congenital meningomyelocele reported in 1949 is cited, in which the child was also affected. The mother had a low lumbar defect with moderate muscular weakness in both legs, but no gross sensory loss and no incontinence. The child had an open myelocele with hydrocephaly and did not survive birth. (1 ref.) - *A. C. Schenker.*

Birmingham Maternity Hospital
Queen Elizabeth Medical Centre
Birmingham B15 2TG, England

2343 **CARTER, C. O.; & EVANS, K. A.** Pregnancy and meningomyelocele. *Lancet,* 1(7796):208, 1973. (Letter)

The claim by Fujimoto and his colleagues that they are the first to report a pregnancy in a woman with a meningomyelocele is contradicted by the citation of other such cases. Tunte reported 2 cases, 1 with spina bifida and 1 with anencephaly, both born to the same patient who was one of a series of men and women with spina bifida "aperta." In a series of 31 women who survived spina bifida and between them had 60 children, one child was affected with anencephaly. Of 24 children born to the surviving men, none was affected. (1 ref.) - *A. C. Schenker.*

M.R.C. Clinical Genetics Unit
London WC1N 1EH, England

2344 **MILHORAT, THOMAS H.; & HAMMOCK, MARY K.** "Arrested" versus normal pressure hydrocephalus in children. *Clinical Proceedings, Children's Hospital National Medical Center,* 28(6):168-173, 1972.

Four children (CA 4½ to 8 years) with naturally "arrested" hydrocephalus showed significantly improved intellectual and motor performance following a ventricular shunting operation, a finding which suggested that this disorder is not a truly physiologic state. Diagnostically, surgically "arrested" and naturally "arrested" hydrocephalus appear to be distinct. In the former, psychomotor development occurs throughout the growth period despite preexisting brain damage if both the primary disorder and resulting hydrocephalus are arrested; in the latter, psychomotor development ceases usually after age 6 to 8. Many children with so-called "arrested" hydrocephalus who fail to demonstrate continued psychomotor development throughout the growth years may be suffering from the syndrome of normal pressure hydrocephalus. (26 refs.) - *B. J. Grylack.*

Children's Hospital
2125 13th Street, N.W.
Washington, D.C. 20009

2345 **MACLEAN, PAMELA R.; PATERSON, W. G.; SMART, G. E.; PETRIE, J. J. B.; ROBSON, J. S.; & THOMSON, D.** Proteinuria in toxaemia and abruptio placentae.

Journal of Obstetrics and Gynaecology of the British Commonwealth, 79(4):321-326, 1972.

Differential protein clearance determinations were made in 31 patients with toxemia and in 21 nontoxemic patients with abruptio placentae, and dextran clearances were studied in 6 patients with toxemia and 7 with abruptio placentae. Renal biopsy was carried out in 20 of the 31 cases, and the obtained tissue was studied by light and electron microscopy. The protein selectivity index was expressed by the symbol -k, representing the change in the logarithm of the clearance per unit change in the logarithm of molecular weight. Selectivity values were determined only in the presence of significant proteinuria. In toxemia, proteinuria was of intermediate selectivity, while in abruptio placentae it was markedly unselective. In toxemia, the values of dextran selectivity were also in the intermediate range, whereas in abruptio placentae the pattern of dextran excretion was highly selective and contrasted sharply with the unselective pattern of protein excretion. The fact that in toxemia both dextran and protein clearances were in the intermediate range suggested that the proteinuria is glomerular in origin and that the glomerular lesions are uniform. In abruptio placentae, the urinary protein is probably postglomerular and is derived from plasma proteins passing through damaged renal tubular epithelium. (26 refs.) - *B. J. Grylack*.

2346 **THOMSON, D.; PATERSON, W. G.; SMART, G. E.; MACDONALD, M. K.; & ROBSON, J. S.** The renal lesions of toxaemia and abruptio placentae studied by light and electron microscopy. *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 79(4):311-320, 1972.

Electron and light microscopic examination of renal biopsies obtained from 33 women on approximately the fourth day postpartum, 20 of them having had toxemia of pregnancy and 13 without preceding clinical evidence of toxemia who had had abruptio placentae, revealed similar findings in both groups. All patients had a characteristic glomerular lesion, slight swelling of and increase in the number of endothelial cells, a slight increase in the amount of mesangial cells and an increase in the amount of mesangial matrix, and deposits of granular, fibrillary, and basement membrane-like material. The lesions were probably of lesser degree in patients with abruptio placentae, but there appeared to be no qualitative difference between the 2 groups. It was suggested that the mesangial and endothelial cell changes seen in toxemia are due to phagocytosis by these cells of fibrin or fibrinogen derivates which have been deposited in the glomerular capillary lumen and that the identical glomerular lesion in abruptio placentae has the same pathogenesis. (33 refs.) - *B. J. Grylack*.

2347 **URSELL, W.** Hydramnios associated with congenital microstomia agnathia and synotia. *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 79(2):185-186, 1972.

A 27-year-old patient hospitalized with hydramnios in the thirty-first week of pregnancy was delivered of a fresh stillborn male infant with gross microstomia, absent mandible, rudimentary buccal lumen, short tongue, absent submandibular and parotid salivary glands, broad and slightly cleft nose, nasal cavity not communicating with the pharynx, and microophthalmia with no eye on the right side. The case may represent an instance of hydramnios due to failure of fetal swallowing. (4 refs.) - *B. J. Grylack*.

Department of Obstetrics and Gynaecology
King's College Hospital
Denmark Hill, London, S.E.5, England

2348 **HALL, MARION H.** Folic acid deficiency and congenital malformation. *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 79(2):159-161, 1972.

In a prospective study the folic acid status in 2,949 singleton pregnancies was assayed at initial prenatal visit and was related to the subsequent incidence of congenital malformation. Among 2,093 parous women, there was a 2% incidence of a positive history of congenital malformation in a previous pregnancy, but the incidence was the same in patients with a low initial serum folate level and in those with a high level. The overall incidence of major malformations in 2,949 singleton pregnancies was 1.6%. There was no significant correlation between low initial serum folate levels and either major or minor fetal malformations. Among patients whose initial visits were made before 12 completed weeks of amenorrhea, there was no trend towards more malformations in those with low serum folate levels, and patients with a

low initial serum folate level before 20 completed weeks of amenorrhea had a lower than average malformation rate. (7 refs.) - *B. J. Grylack.*

University of Aberdeen
Aberdeen, Scotland

2349 **EMERY, A. E. H.; ECCLESTON, D.; SCRIMGEOUR, J. B.; & JOHNSTONE, M.** Amniotic fluid compositon in malformations of the central nervous system. *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 79(2):154-158, 1972.

The hypothesis that in congenital malformations of the central nervous system a leak of 5-hydroxyindole acetic acid (5HIAA) from the central nervous system into the amniotic fluid might occur and thus lead to an increase in amniotic fluid concentration was not supported in a study of amniotic fluid specimens obtained from normal pregnancies at delivery or by transabdominal amniocentesis during the management of rhesus-incompatible pregnancies in which the mother was delivered subsequently of a normal child or from pregnancies terminated for social or psychiatric reasons but producing apparently normal fetuses. Contrary to expectations, levels obtained at least in later pregnancy were less than in controls. Subsequent investigation of 24-hour urinary excretion of 5HIAA in a number of children with spina bifida and CA-matched controls indicated a gradual increase in excretion with increasing age in childhood but no consistent difference between spina bifida and control patients. Reduced 5HIAA levels were not observed in cases of polyhydramnios when the fetus was normal, nor were the levels of other substances present in amniotic fluid less than in normal pregnancies of comparable gestation. Reduced 5HIAA levels in amniotic fluid may result from a relative failure of renal function or could reflect the reduction in functioning neural tissue seen in more severe central nervous system malformations. (13 refs.) - *B. J. Grylack.*

University Department of Human Genetics
Western General Hospital
Edinburgh, Scotland

2350 **MACLENNAN, ALASTAIR H.; SHARP, FRANK; & SHAW-DUNN, JOHN.** The ultrastructure of human trophoblast in spontaneous and induced hypoxia using a system of organ culture. A comparison with ultrastructural changes in pre-eclampsia and placental insufficiency. *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 79(2):113-121, 1972.

Placental villi maintained in organ culture in well oxygenated and hypoxic conditions were compared with normal fresh placental villi collected from patients with uncomplicated pregnancies within the 38- to 41-weeks' gestational period and with villi from a patient showing signs of severe placental insufficiency uncomplicated by hypertensive disease. Tissue response was monitored by electron microscopy, a more sensitive indicator than light microscopy. Definite intracellular changes compatible with the changes of early hypoxia were slight at 48 hours and increased with time. The structural and functional integrity of the trophoblast in 26% oxygen seemed to be maintained fairly well up until 96 hours in organ culture, but hypoxia caused major changes in the trophoblast even at 48 hours. Hypoxia damaged the syncytium, with subsequent attempts at regeneration noted. Changes in preeclampsia were similar to the in vitro changes of hypoxia, but the ultrastructural changes in placental insufficiency, otherwise uncomplicated, showed the most marked resemblance to the experimentally produced changes of hypoxia. The observations suggested that the placental abnormalities seen in placental insufficiency and preeclampsia are the result of hypoxia and not the cause of the hypoxia. (14 refs.) - *B. J. Grylack.*

Glasgow Western Infirmary
Glasgow, W. 1, Scotland

2351 **SHARP, FRANK; CARTY, MATTHEW J.; & YOUNG, HAMISH.** The effects of hypoxia on hydroxysteroid dehydrogenase activity in placental villi maintained in organ culture. *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 79(1):44-49, 1972.

Investigation of hydroxysteroid dehydrogenase (HSD) enzyme activity histochemically in placental villi maintained in organ culture, some under fully oxygenated conditions and some under conditions of hypoxia, demonstrated the significant sensitivity of HSD to conditions of hypoxia, which produced a diminution in HSD activity. Placentae were collected immediately following vaginal delivery from 10 patients with uncomplicated preg-

nancies within the period 38 to 41 weeks' gestation, and each specimen culture was incubated for the presence and localization of histochemically selected HSD and nicotinamide adenine dinucleotide hydrogen diaphorase. Within an apparently selective process, trophoblastic activity was more affected than that in the villous core, and 3β-HSD activity more so than 17β-activity. Within the 17β-HSDs, activity using estradiol-17β as substrate also seemed to be more sensitive than that using testosterone as substrate. The data suggested a relationship between the alterations in villous HSD activity, within the artificial *In vitro* hypoxic conditions of the experiment, and the clinical experience of falling maternal urinary estriol output in cases of significant placental insufficiency. (19 refs.) - *B. J. Grylack.*

University Department of Obstetrics
Queen Mother's Hospital
Glasgow, Scotland

2352 **BULOVA, STEPHEN I.; SCHWARTZ, ELIAS; & HARRER, WILLIAM V.** Hydrops fetalis and congenital syphilis. *Pediatrics*, 49(2):285-287, 1972.

A hydropic infant with syphilis had no evidence of Coombs-positive hemolytic anemia, α-thalassemia, or severe congenital malformations. The infant presented with severe anasarca, ascites, hepatomegaly, splenomegaly, hypoalbuminemia, and anemia, complications seen more commonly in erythroblastosis. The baby did not have the characteristic electrophoretic pattern with 80% or more hemoglobin Barts seen in homozygous α-thalassemia. The onset of hydrops in this case may have resulted from a relatively acute cardiac decompensation secondary to the combination of an acute hemolytic anemia, hypoalbuminemia, and extensive infection. (9 refs.) - *B. J. Grylack.*

Cardeza Foundation for Hematologic Research
Philadelphia, Pennsylvania 19107

2353 **HOSMER, MARION E.; & SPRUNT, KATHERINE.** Screening method for identification of infected infant following premature rupture of maternal membranes. *Pediatrics*, 49(2):283-285, 1972.

Analysis of the concordance or discordance of results of cultures of cord blood, gastric aspirate, and infant blood from infants from whom all 3 specimens were obtained and of cord blood and infant blood from the same infants when the 2 specimens were obtained indicated that the methods used in many insts for screening for infection in infants born of mothers with premature rupture of maternal membranes are inefficient and potentially misleading. Five of 290 infants (less than 2%) had agreement of organism among all 3 cultures. Of the other 14 of 19 infants with positive infant blood cultures, 5 corresponding cord blood and gastric aspirate cultures showed no growth. Of the remaining 9 infants, positive infant blood cultures grew organisms wholly unrelated to cord blood and or gastric aspirate organisms. At least 3 of these infants had clinical evidence of sepsis. Data obtained from infants from whom only 2 cultures were received confirmed the unreliability of the screening system. Routine cultures of cord blood and gastric aspirate should be discontinued, therefore, and infants at risk should be screened routinely for bacteremia and sepsis by cultures of their blood not taken from cord vessels. (2 refs.) - *B. J. Grylack.*

The Babies Hospital
New York, New York 10032

2354 **FANAROFF, AVROY A.; KENNELL, JOHN H.; & KLAUS, MARSHALL H.** Follow-up of low birth weight infants--the predictive value of maternal visiting patterns. *Pediatrics*, 49(2):287-290, 1972.

A retrospective follow-up study was carried out with all infants who had spent more than 14 days in an intensive care nursery and was correlated with the visiting frequency of the mother during the infant's hospital stay. Forty-one of 146 mothers visited their premature infants less than 3 times in a 2-week period. With only 2 exceptions, disorders of mothering occurred exclusively among 38 of these infrequent visitors. Among 36 women who visited and called less than 5 times in 2 weeks, there were 9 disorders of mothering. Visiting patterns and disorders of mothering did not correlate with the possibility of handling their infants within 5 days after delivery accorded to 1 group of mothers or the restriction against touching and feeding their infants until 20 days of age placed on another group of mothers. The study emphasized the importance of visits and phone calls made by parents to the intensive care nursery. (8 refs.) - *B. J. Grylack.*

Babies' and Children's Hospital
Cleveland, Ohio 44106

2355 **CLEMENTS, JOHN A.; PLATZKER, ARNOLD C. G.; TIERNEY, DONALD F.; HOBEL, CALVIN J.; CREASY, ROBERT K.; MARGOLIS, ALAN J.; THIBEAULT, DONALD W.; TOOLEY, WILLIAM H.; & OH, WILLIAMS.** Assessment of the risk of the respiratory-distress syndrome by a rapid test for surfactant in amniotic fluid. *New England Journal of Medicine*, 286(20):1077-1081, 1972.

A relatively simple test was developed for the estimation of pulmonary surfactant in amniotic fluid that is applicable at the bedside. The test was evaluated in double-blind studies in 2 hospitals, each with an obstetric population at considerable risk for infants with respiratory distress syndrome. In 138 samples of amniotic fluid the titer of surfactant was generally low until 30 to 35 weeks' gestation, when it rose sharply. However, the time of appearance of an appreciable titer could vary from 25 weeks to term. Of the infants delivered from 93 of these 138 patients within 24 hours after the test, many were at high risk for idiopathic respiratory distress, and 80 gave clearly positive or clearly negative tests for surfactant. Of these clearly negative at 1/1 dilution, 11 had idiopathic respiratory distress syndrome and 1, transitional respiratory distress. None of the 68 positive at 1/2 dilution had respiratory distress. Intermediate test results indicated a substantial probability that the infant would experience some respiratory difficulty. These data correlated well with the lecithin-sphingomyelin ratio for the prediction of the respiratory distress syndrome. (6 refs.) - *B. J. Grylack.*

University of California
San Francisco, California 94122

2356 **MURDOCK, J. LAMONT; WALKER, BRYAN A.; HALPERN, BARRY L.; KUZMA, JAN W.; & MCKUSICK, VICTOR A.** Life expectancy and causes of death in the Marfan syndrome. *New England Journal of Medicine*, 286(15):804-808, 1972.

Survivorship data on 257 patients with Marfan's syndrome emphasize the unfavorable prognosis in this disease. The probability of survival fell to 0.50 for men in the 40-41-year age group but not until the 48-49-year interval for women. The age for the 48 deceased males was 33.4±15.7 and for the 26 deceased females, 29.5±17.7 years. The ages of the living patients were 21.5±13.1 years for the 99 males and 23.6±15.6 for the 84 females. Aortic problems were the primary cause of death. Although it is still early to draw conclusions about increased survival for patients with the Marfan syndrome treated with propranolol or reserpine, this form of therapy may prolong survival in this group as similar medical therapy has in other forms of aortic dissection. (21 refs.) - *B. J. Grylack.*

Loma Linda University
Loma Linda, California 92354

2357 **NORIEGA-SANCHEZ, ANGEL; MARKAND, OMKAR N.; & HERNDON, JAMES H.** Oculocutaneous melanosis associated with the Sturge-Weber syndrome. *Neurology*, 22(3):256-262, 1972.

Ocular or oculocutaneous melanosis, occurring in association with the Sturge-Weber syndrome, is described in 4 cases. The ocular pigmentary abnormalities observed in the patients involved a sharply demonstrated perilimbal region of the sclerae, the extent of the cutaneous pigmentation varying widely between cases. In case 1 (25-year-old Mexican woman) abnormal pigmentation extended over widespread areas of the face and trunk; in case 2 (the mother of case 1, age 58 years) such pigmentation was restricted to the right periorbital area. Case 4 (a 9-year-old white boy) showed a few patches of increased pigmentation of the face and neck; and in case 3 (a 9-year-old negro girl) the abnormal pigmentation was confined to the sclerae. The abnormal pigmentation in the Sturge-Weber syndrome may be due to developmental defects of the rostral neural tube and underlying mesodermal elements that result in leptomeningeal angiomatosis and cortical atrophy and also cause arrest in the normal migration of melanoblasts with resultant ectopic melanosis. The common association of nevus flammeus in the juxtaocular portion of the face and leptomeningeal angiomatosis overlying the occipital cortex may indicate susceptibility to vascular ectasia appearing early in the embryonic development. The abnormal pigmentation in the cases described resembles nevus flammeus in distribution. (23 refs.) - *A. C. Schenker.*

University of Texas
Southwestern Medical School
Dallas, Texas 75235

2358 **NYHAN, WILLIAM L.** Behavioral phenotypes in organic genetic disease. *Pediatrics Research*, 6(1):1-9, 1972.

Some clinical problems associated with organic genetic disease are illustrated in behavioral features of a number of patients; parallels are drawn to experimental rats and mice and to isolation-reared experimental monkeys. Self-mutilation, a feature of the Lesch-Nyhan syndrome, has been induced in rats, mice, and rabbits by administration of 1,3-methylxanthine or a 1,3-methyl derivative, indicating that some forms of behavior are chemically determined. A pattern of unusual behavior, unique to the de Lange syndrome, has also been demonstrated; circling behavior in children with this disease is associated with the vestibular system. The experimental model with whirling mice demonstrates the results of a developmental defect in their vestibular system detectable as early as the tenth day of fetal life. Other stereotypic behavior seen in these children with genetic disease could reflect structural defects in the central nervous system. Similarities to isolation-reared monkeys are also noted in such sterotypic behaviorisms as rocking and hand posturing. One hyperactive child was found to respond favorably to rotation. None of the patients studied could speak, but communication was possible through gestures. Although stereotypy is common in MR children, patterns observed in the de Lange syndrome seem to be specific. It is suggested that by studying the behavioral patterns of genetic disease, information may be obtained as to underlying deficits. (9 refs.) - *A. C. Schenker.*

University of California, San Diego
La Jolla, California 92037

2359 **GLUCK, LOUIS; KULOVICH, MARIE V.; EIDELMAN, ARTHUR I.; CORDERO, LEANDRO; & KHAZIN, AIDA F.** Biochemical development of surface activity in mammalian lung. IV. Pulmonary lecithin synthesis in the human fetus and newborn and etiology of the respiratory distress syndrome. *Pediatrics Research*, 6(2):81-99, 1972.

Phosphatidyl dimethylethanolamine (PDME) and nonacidic phospholipids were identified in tracheal or orpharyngeal aspirates from full term and prematurely born human infants, both normal and those with respiratory distress syndrome (RDS); diagnosis and prognosis could be established on the basis of the presence or absence of PDME. The Ss were 296 premature (130 with RDS and 166 normal) and 144 full term infants. Aspirates were collected endotracheally under direct laryngoscopy or oropharyngeal suction; lobes of lung from infants who died were analyzed for phospholipids in alveolar wash. Infants with RDS, almost all premature, were observed to have lungs with inadequate surface activity and deficiency in lecithin. Full-term infants are born with 20-40% more β-carbon palmitic acid than RDS infants and have equal palmitic and myristic acids in aspirates as early as 12-18 hr after birth. PDME was identified at 22-24 weeks of gestation; with RDS, PDME disappears and β-carbon palmitic acid increases. When RDS improves, PDME reappears, lecithin increases, and proportions of β-carbon myristic acid increase in acetone-precipitated lecithin in aspirates. Progressive aveolar collapse may initiate atelectasis, anoxia, and acidosis, progressing to death. The RDS is a developmental rather than a disease entity. (34 refs.) - *A. C. Schenker.*

University of California School of Medicine
San Diego
La Jolla, California 92037

2360 **DE MYER, WILLIAM.** Megalencephaly in children: clinical syndrome, genetic patterns, and differential diagnosis from other causes of megalocephaly. *Neurology*, 22(6):634-643, 1972.

Clinical features were determined in patients with megalencephaly in an effort to find criteria for clinical recognition and differential diagnosis. The study was limited to patients with anatomic, rather than metabolic, types of megalencephaly; those for which the essential clinical data are already known were excluded from the study. The criteria for inclusion in the study were: that the occipitofrontal circumference (OFC) exceed 2 standard deviations (SD) above the mean by at least 0.5cm or that the brain weight at autopsy be greater than 1,600gm for mature individuals; that obstructive hydrocephalus, subdural hematomas, or other space-occupying lesions be excluded as the cause for the enlarged head; and that no known metabolic disorder which could cause such abnormality be found. Ss included 18 children; the birthweight was known for 13 Ss and the OFC for 6. The differences of the observed values for weight and OFC from the normal values were

significant. One-half of the Ss were regarded as normal or not definitely MR; the other half of the group was clearly MR. Among the 9 MR children, one had slight hemiparesis, and another had bilateral hyperactive reflexes and extensor toe signs. Other clinical conditions in this group were gigantism, dwarfism, ganglioneuroma, muscular dystrophy, male pseudohermaphroditism, and hypoparathyroidism-hypoadrenocorticism. Males predominated over females (4:1). (45 refs.) - *A. C. Schenker.*

Indiana University Medical Center
Indianapolis, Indiana 46202

2361 Respiratory distress syndrome. *British Medical Journal*, 3(5831):2-3, 1972.

A simple, inexpensive semiquantitative test for estimating the production of pulmonary surfactant and, thus, the likelihood of respiratory distress syndrome has been described in which the ability of the amniotic fluid to form a stable foam is determined in 47.5% ethanol. In a double-blind field trial, 68 infants whose amniotic fluid tested 24 hours before birth gave a positive test at 1/2 dilution were not affected by the syndrome, while 8 of 13 infants with tests positive at 1/1 dilution and negative at 1/2 developed the syndrome. The results correlated well with the lecithin/sphingomyelin ratio. Further study of the surfactant system and of how to influence it pharmacologically is essential in the search for the etiology of this disorder. (16 refs.) - *B. J. Grylack.*

2362 WHITFIELD, C. R.; SPROULE, W. B.; & GREENE, E. M. Respiratory distress syndrome. *British Medical Journal*, 3(5836):362, 1972. (Letter)

The stable-foam test, devised by Clements (1972) to provide a rapid semiquantitative measurement of fetal pulmonary surfactant in amniotic fluid, was clearly positive (at 1/2 dilution) in 76 samples, in 73 of which the lecithin/sphingomyelin ratio was also in the safe zone, but 20 out of 45 clearly negative foam tests were also associated with safe ratios. Further similar findings emphasize that this test should be regarded as a possible simple screening method and that either the lecithin/sphingomyelin ratio or the lecithin concentration should be determined when it is not clearly positive. (2 refs.) - *B. J. Grylack.*

Belfast City Hospital
Belfast, Northern Ireland

2363 GRAZIANI, L. J.; WEITZMAN, E. D.; & PINEDA, G. Visual evoked responses during neonatal respiratory disorders in low birth weight infants. *Pediatrics Research*, 6(4):203-210, 1972.

Summed visual evoked responses (VER) to single and to paired light flashes were studied in 24 low birthweight infants, 13 of whom had respiratory difficulties; the results in the 2 groups were compared for acute abnormalities of cerebral bioelectric function. The VER's were recorded from midline occipital scalp regions during 69 EEG recording sessions. Infants without respiratory difficulty and of less than 36 weeks postconception at the time of recording had VER's which were characterized by a prominent negative wave with a peak latency of 250-350 msec, frequently followed by a smaller positive and negative wave and an inconstant late positive wave at 450-650 msec. When severe hypoxia persisted, complete loss of VER's and an isoelectric EEG or a marked decrease in EEG amplitude were observed in 6 infants, returning to normal VER's following resuscitation in 4 of them, thus indicating that severe EEG abnormalities may be reversible if severe hypoxemia is corrected before permanent brain damage occurs. The results suggest that the VER determinations may be used to monitor the acute effect of hypoxemia on brain electrical activity. (16 refs.) - *A. C. Schenker.*

Thomas Jefferson University
Philadelphia, Pennsylvania 19107

2364 YAMAK, BEHICE; HICSONMEZ, GONUL; OZSOYLU, SINASI; & IMAMOGLU, ILHAN. An infant with Chediak-Higashi syndrome and lymphoma. *Clinical Pediatrics*, 11(5):277-280, 1972.

Autopsy findings in a 13-month-old boy with the Chediak-Higashi syndrome (CHS) showed malignant lymphoma to be already well established. The C-H syndrome is a rare genetic anomaly charac-

terized by partial albinism, photophobia, hepatosplenomegaly, lymphadenopathy, and abnormal leukocytes. While it has long been known that patients with CHS are exceptionally prone to develop lymphoma, this recent finding in a young child suggests that the characteristic infiltration of the tissues with lymphoid cells may develop at a very early stage. (13 refs.) - *N. Mize.*

Ankara University School of Medicine
Ankara, Turkey

2365 CHERNICK, V.; & KARLOWSKY, R. Improvement of the incubator-respirator. *Pediatrics,* 49(5):782-783, 1972. (Letter)

The incubator-respirator was not tested adequately before being marketed. As a result certain modifications have had to be made in order to prevent shipment failure. The medical profession must support strong legislation in the area of electromedical equipment if it wants to avoid this type of occurrence. (1 ref.) - *B. J. Grylack.*

The Children's Hospital
Winnipeg 3, Manitoba, Canada

2366 BHARUCHA, E. P.; PANDYA, S. S.; & DASTUR, DARAB. Arthrogryposis multiplex congenita. I. Clinical and electromyographic aspects. *Journal of Neurology, Neurosurgery, and Psychiatry,* 35(4):425-434, 1972.

Sixteen cases of arthrogryposis multiplex congenita (with limiting deformities in 2 or more joints) were studied. Delayed developmental milestones were found in 15 of 16, and MR in 8. The main deformities were bird-like facies (3 cases), "winging" of the scapulae (5), "policeman tip" contracture of the arms (9), flexed hip (6) or external rotation (2), flexed or extended knees (14), talipes equina (10), pes calcaneus (1), or combined foot defects (1), or "hockey stick" foot (1). Involvement of all limbs was found in 13 of 16. Weakness and wasting were frequent in the shoulder girdle muscles, deep reflexes were unobtainable even in minimally affected limbs, and electromyography revealed neuropathy in 8 of 13 cases. Two yr later, 3 children were reexamined and found to have no improvement in the "policeman tip" arms and poor growth. Although some cases have evidence of neurogenic involvement, the primary defect is probably in muscle formation, particularly in the shoulder region. (16 refs.) - *V. J. Goldberg.*

Children's Orthopedic Hospital
Bombay-8, India

2367 DASTUR, DARAB K.; RAZZAK, ZOHRA A.; & BHARUCHA, E. P. Arthrogryposis multiplex congenita. 2. Muscle pathology and pathogenesis. *Journal of Neurology, Neurosurgery, and Psychiatry,* 35(4):435-450, 1972.

Biopsy material from 16 cases of arthrogryposis multiplex congenita (AMC) included samples from affected and less affected muscles. The affected muscle is characterized by ill-defined fasciculations, small fiber diameter, poor striation, and severe fibrosis. With one exception, intramuscular nerves were not fibrosed, demyelinated, or disorganized. The lesion appears to be a failure of myoblast recruitment from mesenchyme during embryogenesis. Degeneration of spinal motor neurons would result in a lack of neural stimulus for muscle development and is the probable cause of the defects seen in some AMC; disuse atrophy accounts for some of the muscle findings. Proposed pathogenetic mechanisms for AMC include failure to recruit myoblasts from limb-bud mesenchyme by muscle tissue and lack of muscle innervation due to retarded anterior horn cells. (28 refs.) - *V. J. Goldberg.*

JJ Group of Hospitals
Bombay, India

2368 MEHEGAN, CHARLES C.; & *DREIFUSS, FRITZ E. Hyperlexia. *Neurology,* 22(11):1105-1111, 1972.

Exceptional reading ability was noted in 12 otherwise MR children. Incessant, ritualistic reading characterized the dominant behavior which began generally before the age of 5; 2 children exhibited this compulsive trait before the age of 3. Of the 12, only one child was capable of paraphrasing reading material, suggesting perhaps some degree of comprehension. Most of the Ss displayed retarded motor development and all exhibited symptoms of the hyperkinetic syndrome, overactivity, distractibility, and short attention span

when not preoccupied with reading. Marked lack of language development and spontaneous speech were present in all but 3; of these 3, only 1 could be engaged in meaningful conversation. Neurologic examination of the children invariably revealed abnormalities; only 2 had developed right handed dominance and abnormalities in cranial configuration were found in 4. Furthermore, choreoathetosis and multiple bizarre tics were observed; gait and most other motor movements appeared awkward. (12 refs.) - *K. Der.*

University of Virginia School of Medicine
Charlottesville, Virginia 22901

2369 **FRONT, DOV; OVERBEEK, WILLEM J.; & PENNING, LOURENS.** The study of infantile hydrocephalus with combined air and isotope ventriculography. *Journal of Neurology, Neurosurgery, and Psychiatry,* 35(4):456-462, 1972.

A method for combining air and isotope (radioiodinated serum albumin) ventriculography was used for studying suspected cases of hydrocephalus in 29 infants (aged 4 days to 6 mo). A volume of 25 to 60ml of cerebrospinal fluid was exchanged for air and 15μCi of isotope were injected through the fontanelle. Four, 24, and 48hrs later, scintigraphs were made using both the Anger type gamma camera and a rectilinear scanner (thyroid block was achieved with Lugol's iodine). Fifteen had noncommunicating hydrocephalus and of these, 13 had aqueductal stenosis and 2 had occlusions in the foramina of the fourth ventricle. Nine had communicating hydrocephalus with the occlusion in the subarachnoid space at the base of the brain. The causes of hydrocephalus included meningomyelocele (16), subarachnoid hemorrhage (2), meningitis (3), congenital abnormalities (3). Other causes included cyclopean ventricle (1), porencephalic cysts (2), brain abcess (1), and posterior fossa tumor (1). Isotope ventriculography is particularly useful in the diagnosis of communicating hydrocephalus, although air gives better visualization of anatomical structures and topographical localization. A combination of air and isotope gives the best diagnostic results. (16 refs.) - *V. J. Goldberg.*

University Hospital
Gronigen, The Netherlands

2370 **SOMERWILL, LAWRENCE; BROWN, EDWIN G.; & SWEET, AVRON Y.** The incubator-respirator: methods for improving its reliability. *Pediatrics,* 49(5):761-765, 1972.

A modification of the standard infant incubator-respirator along the same lines as that demonstrated by Vidyasagar and Chernick will provide even greater reliability than they have achieved. Relocation of the triac, replacement of a relay with a plug-in system, and revision of the intermittent duty solenoid have eliminated overheating and reduced deterioration of other valuable operating components. (3 refs.) - *B. J. Grylack.*

Cleveland Metropolitan General Hospital
Cleveland, Ohio 44109

2371 **CHERNICK, V.; & VIDYASAGAR, D.** Continuous negative chest wall pressure in hyaline membrane disease: One year experience. *Pediatrics,* 49(5):753-760, 1972.

Application of a continuous positive transpulmonary pressure by producing a continuous negative chest wall pressure (CNP) in the case of 49 infants with severe hyaline membrane disease seemed to reveal 2 distinct infant populations. In 23 patients whose alveolar ventilation was sufficient to maintain arterial Po_2 below 70mm Hg, CNP was associated with an average elevation in arterial Po_2 of over 40mm Hg, whereas inspired oxygen concentration remained unchanged. The calculated alveolar-arterial Po_2 difference ($A\text{-}aDo_2$) was very high prior to therapy and fell by 70mm Hg ($p<.001$). All of these infants survived as compared with only 12 of the 26 with severe alveolar hypoventilation. In these infants, use of CNP together with artificial ventilation led to a significant increase in arterial Po_2 and a decrease in $A\text{-}aDo_2$. The overall survival rate for this series was 35 of 49 patients, or 71.5%. Although every method used thus far has disadvantages, the marked improvement seen in the clinical course of infants with hyaline membrane disease indicates that at least 1 method of applying a continuous transpulmonary pressure should be used. (6 refs.) - *B. J. Grylack.*

Children's Hospital
Winnipeg 3, Manitoba, Canada

2372 **HOBEL, CALVIN J.; HYVARINEN, MARCIA A.; & OH, WILLIAM.** Abnormal fetal heart rate patterns and fetal acid-base balance in low birth weight infants in relation to respiratory distress syndrome. *Obstetrics and Gynecology*, 39(1):83-88, 1972.

The abnormal heart rates observed in 15 of 25 fetuses (650-2500g) during labor were correlated with low Apgar scores, decreased arterial and venous blood pH, increased $PaCO_2$, and base deficits. Ten of 15 abnormal heart rate infants vs 1 of 10 normal infants had RDS. Among infants weighing more than 1500g, 6 of 11 with an abnormal heart rate and 1 of 9 with a normal heart rate had RDS. The data support the hypothesis that acidosis in the perinatal period contributes to the initiation of RDS. Monitoring of fetal heart rate and fetal acid-base balance may help detect low birthweight infants at risk for RDS. (13 refs.) - *V. J. Goldberg.*

Harbor General Hospital
Torrance, California 90509

2373 **BLAND, RICHARD D.** Cord-blood total protein level as a screening aid for the idiopathic respiratory distress syndrome. *New England Journal of Medicine*, 287(1):9-13, 1972.

Umbilical cord blood total protein determinations, using the TS meter method, were made on samples from 2,200 neonates. There were 34 cases of idiopathic respiratory distress, resulting in 19 deaths. Protein levels for infants with IDS were 3.80±0.61g/100ml vs 5.91±0.70 for those without IDS ($p<0.001$) and 4.08±0.65 and 3.58±0.51 for IDS survivors and fatalities, respectively ($p<0.01$). IDS developed in 0.5% infants with protein levels above 4.6g/100ml, regardless of maturity or birthweight, while one-half of those with low protein levels, immaturity, or low birthweight developed IDS. These findings suggest that the cord protein level can be used to screen low birthweight infants at risk for IDS. (25 refs.) - *V. J. Goldberg.*

Tripler Army Medical Center
Honolulu, Hawaii

2374 **KANDALL, STEPHEN R.** Congenital pulmonary lymphangiectasis. *Clinical Pediatrics*, 11(2):107-111, 1972.

The need to consider congenital pulmonary lymphangiectasis (CPL) in the differential diagnosis of both acute and chronic respiratory distress in the newborn period is emphasized by a recent experience with a CPL infant who survived for 25 days. As reports come in, it is becoming clear that the CPL diagnosis properly encompasses a whole spectrum of neonatal and infantile lung disease. The condition is almost uniformly fatal and is characterized by lung restriction and alveolar hypoventilation secondary to marked lymphatic dilatation. Term infants are most often affected; symptoms begin at birth, with cyanosis an early feature. Lung biopsy is the only definitive means of establishing a CPL diagnosis since, especially if the infant survives the first few days, the condition is easily confused with other respiratory syndromes. (9 refs.) - *N. Mize.*

University of California
Medical Center
San Francisco, California 94122

2375 **KARPATKIN, MARGARET; SACKER, IRA; & ACKERMAN, NEIL.** Respiratory-distress syndrome and disseminated intravascular coagulation in two siblings. *Lancet*, 1(7741):102-103, 1972. (Letter)

Two occurrences of idiopathic respiratory distress syndrome (IRDS) and disseminated intravascular coagulation (DIC) in infants born a year apart to the same parents are reported. The appearance of the complications followed a similar course in each, with death occurring at 36 hrs in the first and at 10 days, following extensive heparin treatment, in the second. Both cases are clinically unusual in that the infants were not premature and were of normal weight. No maternal factors which would predispose to this condition could be discovered. It seems possible that the children exhibiting this apparently new syndrome may have lacked some normal *in vivo* mechanism for inhibiting coagulation. If this is the case, the DIC might have been prevented during intrauterine life because the missing inhibitor was derived transplacentally from the mother. (3 refs.) - *N. Mize.*

New York University School of Medicine
New York, New York 10016

2376 **PARK, I. JAMES; JOHANSON, ANN; *JONES, HOWARD W.; & BLIZZARD, ROBERT.** Special female hermaphroditism associated with multiple disorders. *Obstetrics and Gynecology,* 39(1):100-106, 1972.

A 16-yr-old female with a 46,XX karyotype exhibited many congenital anomalies including ambiguous external genitalia, double vagina, bicornuate uterus, anomalous position of the urethral orifice, congenital central deafness, lack of speech, ectodermal defects, athyreotic cretinism, pancreatic achylia, MR, and primordial dwarfism. It is not known whether this patient and others with the same type of nonadrenal female hermaphroditism have the same underlying disorder or represent, instead, several disorders having in common an anomalous development of the external genitalia. (17 refs.) - *V. J. Goldberg.*

*Johns Hopkins School of Medicine
Baltimore, Maryland 21205

2377 **ANDRIOLA, MARY; & STOLFI, JOSEPH.** Sturge-Weber syndrome. *American Journal of Diseases of Children,* 123(5):507-510, 1972.

An 11-yr-old boy exhibited an atypical form of the Sturge-Weber syndrome in that the usual facial nevus, glaucoma, and MR were absent. At age 11 mos, he had generalized seizures with focal onset, normal EEG, and subsequent left foot drag. At age 6, the seizures became more frequent and the EEG was abnormal. At age 9 the child exhibited an IQ of 80, daily seizures preceded by a visual aura, abnormal EEG, and normal brain scan, pneumoencephalogram, and angiography. Skull X-ray showed the characteristic sinuous double lined calcifications in the right parietooccipital area, and there was a complete homonymous hemianopsia in the visual field examination. These findings are compatible with the Sturge-Weber syndrome. (14 refs.) - *V. J. Goldberg.*

1542 Tulane Avenue
New Orleans, Louisiana 70112

2378 **RENWICK, J. H.** Spina bifida, anencephaly, and potato blight. *Lancet,* 2(7784):967-968, 1972. (Letter)

Contrary to the impression given by Dr. Emanuel, the very low incidence of spina bifida in Taiwan agrees well with the low potato consumption there and thus is consistent with the potato-avoidance hypothesis. It is becoming increasingly difficult to escape the conclusion that the substance to be avoided to prevent spina bifida is not exactly the same as the one to be avoided to prevent anencephaly, although both may be carried in the same diseased potato. Just as in Britain, where the poorer housewife tends to discard fewer potatoes than the richer housewife, so in Taiwan she discards less rice. Thus, it is the quality of foodstuffs rather than the quantity that correlates well with malformation rates. Support has been found for the hypothesis that anencephaly and spina bifida are 95% preventable by avoidance of specific but unidentifiable substances present in certain potato tubers, the identification of which may be achieved within the next 3 years. (13 refs.) - *B. J. Grylack.*

London School of Hygiene and Tropical Medicine
London WC1E 7HT, England

2379 **ZACHARY, R. B.** The improving prognosis in spina bifida. *Clinical Pediatrics,* 11(1):11-14, January 1972.

Many factors in the management of spina bifida have been responsible for the greatly improved prognosis over recent years with respect to both morbidity and survival. Early shunt operations and increased attention to the prevention and treatment of CNS infection have contributed not only to the greater survival rate but to substantial improvement in the quality of life for each individual patient as well. Additionally, surgical treatment of the open myelomeningocele and of the paralytically dislocated hip has greatly improved the prospects for ambulation in many cases. Renal tract dysfunction has been substantially improved by advances in operative technique and by other procedures especially designed to establish an unobstructed outflow of urine. As a result of all these basic advances in management, children with spina bifida are showing striking improvements in personality and school performance and are being allowed to come much closer to the realization of their full potential. - *N. Mize.*

The Children's Hospital
Sheffield S10 2TH, England

2380 LAURENCE, K. M. Potato blight teratogen. *Nature*, 240(5383):579-580, 1972. (Letter)

The theory proposed previously by Renwick that the damaged or diseased and, especially, the blight-diseased or even blight-resistant potato is in some way related etiologically to anencephaly and spina bifida cystica is unacceptable. The time/space relationship cited between secular changes in malformation rates and the severity of blight in West Scotland, the United States, and other places is not close everywhere in the British Isles. Additionally, central nervous system malformations are found in parts of the world where potatoes are not consumed. It is likely that not a single teratogen malformation but one which is multifactorial is at issue. The climate of opinion being created among the general public by the great amount of publicity given to the theory is making it very difficult to conduct a properly randomized and controlled trial of potato avoidance in susceptible women who plan a pregnancy and have previously had a child with spina bifida or anencephaly. - *B. J. Grylack.*

Llandough Hospital
Penarth, Glamorgan CF6 1XX, Wales

2381 ANDREASEN, CHRISTIAN B. Isolette respirator modification for constant negative pressure. *Pediatrics*, 49(6):922, 1972. (Letter)

Air-Shields, Inc., is offering to all owners of Isolette Respirators a modification kit, incorporating many of the recommended changes, in order to improve the reliability of these units. The kit reflects the responsibility of Air-Shields to provide equipment that is safe, reliable, and effective. Federal legislation which will not inhibit or discourage the new product development process is welcomed. (3 refs.) - *B. J. Grylack.*

Air-Shields, Inc.
Hatboro, Pennsylvania 19040

2382 FARRELL, PHILIP M.; & ZACHMAN, RICHARD D. Corticosteroids as primary therapeutic agents in respiratory distress syndrome (RDS). *Pediatrics*, 51(5):952-954, 1973. (Letter)

Some comments are offered on the article by Liggins and Howie on the supportive management, using corticosteroids, for antepartum respiratory distress syndrome (RDS) in infants. The fact that beneficial intervention was accomplished by the authors only in the case of premature infants of 26-32 wk gestation and not for those of more than 32 wk, might be explained by some results published by Gluck, which suggest that in humans the choline incorporation pathway of lecithin synthesis becomes effective later in gestation (beyond 35 weeks). The effect of cortisol in the 26-32-week fetus is to induce or enhance the rate of the pathway, with resultant surfactant synthesis. It is suggested that a more appropriate schedule of hydrocortisone administration would be at 6-hour intervals for the first 3-4 days of the disease, rather than the schedule suggested by Baden. (16 refs.) - *A. C. Schenker.*

Pediatric Metabolism Branch
National Institutes of Health
Bethesda, Maryland

2383 ULRICH, A. FRANK; BORDIUK, JOSEPH M.; BORROMEO-MCGRAIL, VIRGINIA; SALTZMAN, MARCUS B.; & KEITEL, HANS G. Treatment of apnea in neonates with an automated monitor-actuated apnea arrestor. *Pediatrics*, 51(5):878-883, 1973.

A monitor-triggered automatic apnea arrestor is described for stimulating neonates; 11 methods of stimulation are compared. The methods tested in a population of 38 infants included visual, auditory, thermal, and mechanical balloon models, these being placed in different positions with reference to the infant's body. Each stimulus was applied 3 times and started with the S asleep; it was discontinued when the infant became excessively alert. The response was evaluated by observation of body movements. The mechanical method which proved most effective over all other 10 methods was one in which a rapidly inflated and deflated balloon was placed under the infant's neck, evoking a startled response, and was thus used as a model for treating apnea. A combination monitor-apnea arrestor equipment system detected and applied a counteracting stimulus in 105 apneic episodes in 4 low birthweight patients; on 99 occasions the apnea was arrested. (12 refs.) - *A. C. Schenker.*

Hoffmann-La Roche Inc.,
Cranbury, New Jersey 08512

2384 **REYNOLDS, JOHN W.** Serum total corticoid and cortisol levels in premature infants with respiratory distress syndrome. *Pediatrics*, 51(5):884-890, 1973.

Since hyposecretion of steroids has been implicated in hyaline membrane disease (HMD), a study was undertaken to evaluate postnatal adrenal cortical function in premature infants with respiratory distress syndrome of varying degrees of severity. Three groups were studied: 15 Ss with fatal HMD, 13 with nonfatal HMD, and 16 with benign respiratory distress (BRD). Blood samples were obtained from indwelling catheters; 9 infants underwent adrenal stimulation by ACTH, and a post stimulation sample was obtained. The results showed that the infants with fatal HMD had significantly higher ($p<.001$) total corticoid and cortisol levels than the infants with BRD, both in the first 3 days of life and in infants over 7 days of age. Infants in all 3 diagnostic categories responded to adrenal stimulation by cosyntropin. There is no evidence that postnatal adrenal cortical hypofunction plays a role in the pathogenesis of HMD; the high cortisol levels of infants with fatal HMD probably reflect a response to stress. (16 refs.) - *A. C. Schenker.*

Children's Hospital
St. Paul, Minnesota 55102

2385 **HOLM, WILLIAM W.** Corticoid and respiratory disease. *Pediatrics*, 51(5):955-956, 1973. (Letter)

Reference is made to Liggins and Howie's article on the effect of antepartum dexamethasone in the prevention of the respiratory distress syndrome (RDS). It is suggested that the mature infant responds to stress with an epinephrine mediated catecholamine response whereas the infant *in utero* and the immature infant with RDS react with a norepinephrine mediated response. This response produces pulmonary artery vasoconstriction, pulmonary perfusion via the bronchial arteries, and decreased peripheral circulation permitting the infant *in utero* more efficient placental perfusion; however, in the immature newborn it produces pulmonary hypoperfusion and the finding of RDS. Dexamethasone is a potent inducer of ethanolamine-n-methyltransferase in the methylation of norepinephrine to epinephrine. Antenatal administration of this corticoid matures the adrenal and provides the infant with an epinephrine mediated catecholamine response for extrauterine existence. This hypothesis may explain the effective response to dexamethasone in the 28-55-wk-old infant with RDS. (10 refs.) - *A. C. Schenker.*

419 Allendale Road
King of Prussia,
Pennsylvania 19406

2386 **LEONIDAS, JOHN C.; HALL, ROBERT T.; HOLDER, THOMAS M.; & AMOURY, RAYMOND A.** Pneumoperitoneum associated with chronic respiratory disease in the newborn. *Pediatrics*, 51(5):933-935, 1973.

Pneumoperitoneum associated with chronic pulmonary disease but in the absence of gastrointestinal perforation and no detectable mediastinal or pleural air, is described in a premature infant. She was the product of a 26-week gestation weighing 800gm, and was transferred to the children's hospital because of prematurity and respiratory distress. The patient received oxygen under a hood but began having frequent episodes of apnea and bradycardia and by the fourth hospital day had to be placed on a respirator. X-rays revealed progressively severe pulmonary disease, typical of disseminated focal atelectasis and emphysema. On the eighteenth day abdominal films showed pneumoperitoneum. Surgery was performed because of suspected gastric perforation, but this was not the case. The infant died on the twenty-fourth day. Autopsy revealed focal subarachnoid and subependymal hemorrhages of the central nervous system and acute confluent bronchopneumonia. The pattern of bowel gases should be examined on roentgenograms for signs of necrotizing enterocolitis in such cases, and contrast examinations of the upper gastrointestinal tract and colon are recommended to document the presence or absence of perforation. (9 refs.) - *A. C. Schenker.*

Children's Mercy Hospital
Kansas City, Missouri 64801

2387 **PENA, SERGIO DANILO JUNHO; & *GOODMAN, HAROLD O.** The genetics of thanatophoric dwarfism. *Pediatrics*, 51(1):104-109, 1973.

Thanatophoric dwarfism is described in 2 cases, and several genetic hypotheses are reviewed in

connection with its etiology and diagnostic guidelines. In classical achondroplasia the limbs are longer and neonatal deaths are uncommon, compared with thanatophoric dwarfism. A further distinction is that in the former, the long bones are not curved and the metaphyseal irregularities are less marked. The cartilage cells in achondroplasia have an orderly columnar arrangement in contrast to the disorderly arrangement in thanatophoric dwarfism and achondrogenesis. In the latter, the head is larger and body length is less than in thanatophoric dwarfism. Differential diagnosis must thus depend on radiologic signs. Data are compatible with autosomal recessive inheritance only if one assumes some considerable fraction of spontaneous abortion represent affected cases. The hypothesis of polygenic inheritance requires fewest assumptions. (28 refs.) - *A. C. Schenker.*

*Wake Forest University
Winston-Salem, North Carolina 27103

2388 **LEMIRE, RONALD J.; BECKWITH, J. BRUCE; & SHEPARD, THOMAS H.** Iniencephaly and anencephaly with spinal retroflexion. A comparative study of eight human specimens. *Teratology*, 6(1):27-36, 1972.

The morphological features of 8 embryos and fetuses with retroflexion of the upper spine including examples of iniencephaly and anencephaly are presented. The distinction between iniencephaly clausus and anencephaly is related to the time of onset; the latter, in which cranial nervous tissue is directly exposed to the surface, occurs prior to closure of the cephalic neural folds in Horizon XI 24 days' gestational age. Malformations with uninterrupted skin covering, which is the case in iniencephaly, occur after the cephalic neural tube closure. The major factors common to both types of malformations include: elongation of arms, defects in development of diaphragm, anomalies of thoracic cage, hypoplasia of certain organs, and anterior spina bifida. The most important of the dissimilar features is cranioschisis which is related to the time of onset and clearly separates the lesions temporally. The difference in this time of onset may be only a few days, as evidenced by the frequent occurrence of myeloschisis of the spine in iniencephaly. (29 refs.) - *A. C. Schenker.*

University of Washington School of Medicine
Seattle, Washington 98195

2389 **MACE, JOHN W.; & GOTLIN, RONALD W.** Short stature and onychodysplasia: report of a case resembling Senior syndrome. *American Journal of Diseases of Children*, 125(1):114-116, 1973.

Counseling of juvenile Senior syndrome patients should be conservative as to eventual height expectation. A 16.5-year-old patient with clinical features resembling Senior syndrome (short stature with antenatal onset, onychodysplasia, and digital anomalies), and with the additional features of shortened fourth metatarsals with abnormally placed fourth toes, abnormal shortness of stature when fully grown, and a marked acceleration of bone maturation during puberty, had been destined, according to Greulich and Pyle Prediction Tables, to reach an adult height of 62 inches. Comparison of bone age films of the S taken at 11 yrs 2 mos and at 16 yrs 6 mos showed that skeletal maturation had advanced 9.5 yrs in only a 5 yr period, without concomitant increase in growth rate. Height of the S had only increased from 48 to 56 inches. Such disordinate maturation and growth rates have not previously been associated with any disorder but those of androgen or estrogen excess, but the S showed no evidence of an endocrine imbalance and has received no exogenous hormones. Treatment trials with anabolic agents might be considered for such Ss. (5 refs.) - *C. Wares.*

Loma Linda (Calif.) University School of Medicine
Loma Linda, Calif.

2390 ***WELCH, K. M. A.; MEYER, JOHN STIRLING; TERAURA, TETSUAKI; HASHI, KAZUO; & SHINMARU, SEIJI.** Ischemic anoxia and cerebral serotonin levels. *Journal of the Neurological Sciences*, 16(1):85-92, 1972.

Changes in cerebral arteriovenous (A-V) differences for serotonin (5-HT) levels during acute ischemic anoxia of the brain stem and cerebral hemispheres, induced by serial occlusion of the vertebral and carotid arteries, were studied in 12 baboons; a possible relationship to cerebrovascular disease in humans was investigated. The results indicated that 5-HT may be released from the brain into the cerebral venous blood when both vertebral arteries are occluded, presumably due to ischemic damage to the nuclei of the median raphe where most of the nuclei of 5-HT containing

neurons are located. During 4-vessel occlusion, platelets presumably accumulate in the cerebral vessel and may release 5-HT into the plasma or the brain during the process of aggregation. Widening in cerebral A-V differences was too extensive to be attributed to failure in an active transport mechanism alone. The evidence suggests that 5-HT accumulates in brain and CSF as a result of ischemic anoxia. The study supports the concept that increased levels of 5-HT in CSF and brain of patients with acute cerebrovascular disease may be an important contributory factor to the etiology of serious and fatal complications. (31 refs.) - *A. C. Schenker.*

*Baylor College of Medicine
Houston, Texas 77025

2391 **MILLER, MARILYN E.; RORTH, MICHAEL; PARVING, H. H.; HOWARD, DONALD; REDDINGTON, IRENE; VALERI, C. R.; & STOHLMAN, FREDERICK, JR.** pH effects on erythropoietin response to hypoxia. *New England Journal of Medicine*, 288(14):706-710, 1973.

The effects of hypoxia on erythropoietin were studied in human volunteers who were exposed to hypoxia in a control state and following treatment with acetazolamide. The Ss comprised 6 healthy males (20-25 years of age); they were exposed to a simulated altitude of 4,500 meters for 24 hr in a decompression chamber. Arterialized capillary blood, venous blood (obtained anaerobically), and urinary samples were collected at various intervals, including pre-exposure samples. Three healthy male volunteers were also given acetazolamide. Respiratory alkalosis developed immediately following exposure to the hypoxic stress of 4,500 meters. After initiation of exposure, there was a slow accumulation of intraerythrocytic 2,3-diphosphoglycerate, which decreased the oxygen affinity of the red cells, thus favoring oxygen delivery to the tissues. Treatment of Ss before and during exposure to high altitude with acetazolamide prevented the respiratory alkalosis. It is possible that pH has a direct effect on the cells producing erythropoietin. The reduced capacity to produce erythropoietin in the anephric state may reflect, besides the loss of tissue that normally produces this substance, also changes in acid base, altering oxygen delivery to extrarenal states. (32 refs.) - *A. C. Schenker.*

St. Elizabeth's Hospital
736 Cambridge St.
Brighton, Massachusetts 02135

2392 **HOEFNAGEL, D.; WURSTER, D.; CAREY, D.; HARRIS, G. J.; & PILLIOD, J.** Camptomelic dwarfism. *Lancet*, 1(7759):1968, 1972. (Letter)

A healthy 23-year-old mother recently gave birth to a female infant, of normal karyotype, who exhibited the camptomelic dwarfism syndrome. The infant survived for 5 days. Clinical and radiological features, including large head, retrognathia, low-set ears, and bowing of the long bones, were typical of this syndrome. Since the mother had no history of using contraceptive drugs, this source is eliminated as a possible teratogenic factor. In light of this, the condition should generally be regarded as a distinct syndrome of unknown cause and should be added to the list of constitutional bone diseases manifested at birth. (9 refs.) - *N. Mize.*

Dartmouth-Hitchcock Medical Center
Hanover, New Hampshire 03755

2393 Cor leopardum. *Journal of the American Medical Association*, 220(9):1239, 1972. (Editorial)

While diagnosis of the "little leopard" syndrome in children is not difficult, the cardiac involvement which is part of the classical lentiginosis picture is frequently overlooked or misdiagnosed. In the past, the early cardiac symptoms and signs in these patients have often led to a preliminary diagnosis of pulmonary stenosis. More recently, a review of these cases and of others indicates that the characteristic lesions seen in cases of the leopard syndrome are, in fact, those of cardiomyopathy. Other enzymatic and metabolic derangements of the leopard syndrome, which is characterized clinically by lentigo, short stature, MR, ocular defects, abnormal genitalia, deafness, and congenital heart defects, remain still to be deciphered. (3 refs.) - *N. Mize.*

2394 **GOODLIN, R.** Fetal heart rate patterns. *Journal of the American Medical Association*, 220(7):1015, 1972. (Letter)

From experience with 1,750 parturients in late

labor, fetal heart rate analysis based on the deceleration concept of interpretation recommended by Schrifton has resulted in an excessive number of false diagnoses of fetal distress and has, because of this, been discontinued by the author. Nearly 4½ times as many fetuses in distress were diagnosed by this method as proved actually to be in distress on the basis of Apgar score and overall newborn condition. This high incidence of false diagnosis should clearly negate the "deceleration" concept. A more useful indicator of fetal distress is the pattern of base line variability which, with a fetus in good condition, will remain consistently variable. - *N. Mize.*

Stanford University Medical Center
Stanford, California

2395 **ALEXANDER, JOHN P.; & FRAZER, MURIEL J. L.** Meteorism during treatment of respiratory-distress syndrome by intermittent positive-pressure ventilation. *New England Journal of Medicine,* 288(23):1246, 1973. (Letter)

The description of 3 adult patients in whom meteorism developed in connection with postoperative ventilatory assistance through a nasotracheal tube prompted a report of a similar occurrence in a neonate. The patient was a 2,800gm female neonate who was delivered at term by cesarean section and developed respiratory distress a few hours later. Intermittent positive-pressure was instituted 24 hr after birth via a nasotracheal tube because of deteriorating clinical and biochemical findings; a small positive pressure was maintained during expiratory phase. Abdominal distension and cyanosis developed 18 hr later, and X-ray revealed a right-sided pneumothorax and meteorism. The chest was drained and a gastric tube passed; intermittent positive pressure was maintained for 58 hr, followed by continuous positive airway pressure for 20 hr. The situation was thus relieved by passage of a gastric tube. (3 refs.) - *A. C. Schenker.*

Belfast City Hospital
Belfast, Northern Ireland

2396 **KLEIN, MAX.** Asphyxia neonatorum caused by foaming. *Lancet,* 1(7760):1089-1091, 1972.

A foaming syndrome exhibited by 12 apparently healthy newborns, 11 of whom had been delivered by cesarean section, may be caused by the absence of an effective chest squeeze in labor. Typically, the infants became apneic after taking their first vigorous breaths and were asphyxiated by profuse foam obstructing the airway. All recovered fully following resuscitation. It is probable that the vigorous mixing of the surfactant-rich fetal lung fluid with air during the babies' first cries led to the foaming. A similar syndrome has previously been observed in animals delivered by cesarean section. (10 refs.) - *N. Mize.*

University of Cape Town Medical School
Cape Province, South Africa

2397 **CRUISE, MARY O.** A longitudinal study of the growth of low birth weight infants: 1. Velocity and distance growth, birth to 3 years. *Pediatrics,* 51(4):620-628, 1973.

As part of a longitudinal study of low birthweight infants, to establish satisfactory norms of velocity growth, data are presented on velocity growth of such children during the first 3 years of life. The Ss comprised 202 single-birth, Caucasian, healthy, low birthweight infants; each of the 115 females and 87 males weighed less than 2,500gm at birth. Group 1 comprised infants of gestational age 28-32 weeks. Velocity and distance growth in weight, length, and head circumference were analyzed. Group III had the largest mean measurements at birth ($P<.01$), but by 1 year of age these infants were surpassed in velocity and distance growth by those of Groups I and II. The velocity growth of each study group of infants was greatest during the first 3 months of life; differences in growth of head circumferences were particularly marked in the higher velocity growth of Groups I and II as compared with Group III. Comparative infants of each sex continued to maintain larger mean measurements than low birthweight infants through 3 years of age ($P<.01$), except for head circumference of males. (59 refs.) - *A. C. Schenker.*

Children's Hospital of Buffalo
Buffalo, New York 14222

2398 **HOLMES, LEWIS B.; NASH, ANDREA; ZuRHEIN, GABRIELE; LEVIN, MICHAEL; & OPITZ, JOHN M.** X-linked

aqueductal stenosis: clinical and neuropathological findings in two families. *Pediatrics,* 51(4):697-704, 1973.

Unusual neuropathological findings are reported in 2 infants with X-linked aqueductal stenosis. The abnormal aqueducts in these patients were similar to the patient described by Edwards: all were stenotic throughout, the greatest stenosis being at the inferior constriction. Forking of the aqueduct distinguishes the 2 cases from other X-linked aqueductal stenosis and is commonly found in neonates with hydrocephalus due to aqueductal stenosis. The possibility of X-linked stenosis of the aqueduct of Sylvius should be considered in all congenitally hydrocephalic males without meningomyelocele. In counseling these families, it is important first to have proof of the anatomic nature of the obstruction; an analysis of the family history is important to distinguish between the stenosis that occurs sporadically and that which is due to the X-linked gene for aqueductal stenosis. (20 refs.) - *A. C. Schenker.*

Massachusetts General Hospital
Boston, Massachusetts 02114

2399 **O'BOYLE, MEADE P.; FLETCHER, ANNE B.; & *AVERY, GORDON B.** Objective early criteria for ventilatory assistance in hyaline membrance disease. *Pediatrics,* 51(4):748-749, 1973.

Blood gas data from 36 patients with hyaline membrane disease (HMD) were examined retrospectively to determine if there are criteria observable in the first 24 hours of life which can reliably predict whether the baby will require artificial ventilation. Current results with continuous positive airway pressure (CPAP) are so promising, that if it could be instituted early for those who require it, exposure to toxic concentrations of oxygen could be avoided. The retrospective analysis of blood gases revealed that in the first 26 hours of life, an arterial oxygen tension (PaO_2) of 45mm Hg or less in an inspired oxygen concentration (FiO_2) of 60% identifies most babies who will ultimately require ventilatory assistance. (7 refs.) - *A. C. Schenker.*

*Children's Hospital of the
District of Columbia
Washington, D.C. 20009

2400 **MERENSTEIN, GERALD B.** Fetal monitoring and neonatal blood loss: was transfusion indicated? *Pediatrics,* 51(4):756, 1973. (Letter)

In Scanlon and Walkley's article identifying another iatrogenic neonatal anemia, it is difficult to understand why this infant was not transfused. The infant described may well have had type B and type C hypoxia; these have been defined by Duc as hypoxia with hypoxemia due to a decrease in blood oxygen content without a decrease in PaO_2, and hypoxia with normoxemia due to a decrease in peripheral blood flow, respectively. The finding of significant anemia or hypotension warrants consideration for immediate transfusion to maintain normal blood pressure and prevent anemic hypoxia. (3 refs.) - *A. C. Schenker.*

Fitzsimmons General Hospital
Denver, Colorado 80240

2401 **BANCALARI, EDUARDO; GARCIA, OTTO L.; & JESSE, MARY JANE.** Effects of continuous negative pressure on lung mechanics in idiopathic respiratory distress syndrome. *Pediatrics,* 51(3):485-493, 1973.

The effects of continuous negative chest wall pressure (CNP) upon the mechanics of breathing and on pulmonary circulation in patients with idiopathic respiratory distress syndrome (IRDS) were studied. Subjects were 12 newborn infants with IRDS. No significant change occurred in pH, arterial blood bicarbonate concentration, or arterial blood carbon dioxide tension. Arterial blood oxygen tension increased in all cases except one. Respiratory rate decreased slightly in all cases and the tidal air fell, resulting in a significant reduction in minute ventilation ($P<0.001$). Lung compliance decreased, while functional residual capacity increased. The drop in ventilation produced with the negative pressure may be due to a possible reduction in dead space ventilation or to an increase in the work of breathing due to a reduction in lung compliance. The decrease in dynamic compliance during CNP is particularly significant because the respiratory rate and the tidal volume decreased, both changes tending to increase dynamic compliance; the decrease seen may be explained by an overexpansion of ventilated units, in addition to the recruitment of

previously collapsed alveoli. (22 refs.) - *A. C. Schenker.*

University of Miami School of Medicine
Miami, Florida 33152

2402 **SIEGEL, SHARON R.; PHELPS, DALE L.; LEAKE, ROSEMARY D.; & OH, WILLIAM.** The effects of rapid infusion of hypertonic sodium bicarbonate in infants with respiratory distress. *Pediatrics,* 51(4):651-654, 1973.

The effects of rapid hypertonic sodium bicarbonate infusion for the correction of metabolic acidosis in neonates with respiratory distress were studied for changes in the central nervous system. The Ss were 18 premature and full-term newborn infants with predominant metabolic acidosis associated with respiratory distress following asphyxia neonatorum (1 S), interstitial emphysema and/or pneumothorax (4 Ss), and respiratory distress syndrome (13 Ss). An intravascular infusion of 0.9 M sodium bicarbonate was given at a mean single dose of 2.8mEq/kg, at a rate of 2ml/min. The hematocrit fell at 3 min postinfusion from 50% to 45 and then rose to 46.5% at 30 min; both changes were significant. Serum sodium rose significantly from 135 to 141mEq/liter at 3 min, returning to 136mEq/liter at 30 min. Osmolality increased significantly from 278 to 287mOsm/liter at 3 min, returning to 281mOsm/liter at 30 min; and mean arterial blood pressure rose from 46 to 48mm Hg at one min, remained at this level for 3 min, dropped to 44 at 15 min, and rose to 45mm Hg at 30 min. The fluid shifts and electrolyte changes in these infants are similar in direction to those in experimental animals who had shown central nervous system (CNS) changes, but the rate of infusion was slower in the babies, and no clinical symptoms of CNS changes were evident. (12 refs.) - *A. C. Schenker.*

Harbor General Hospital
Torrance, California 90509

2403 **CUMARASAMY, NILOUFER; NUSSLI, ROSMARIE; VISCHER, DIETER; DANGEL, PETER H.; & *DUC, GABRIEL V.** Artificial ventilation in hyaline membrane disease: the use of positive end-expiratory pressure and continuous positive airway pressure. *Pediatrics,* 51(4):629-640, 1973.

A summary of experience with artificial ventilation in patients with hyaline membrane disease during a period of 3 years is presented. A total of 120 patients were studied (1969 through 1971), of whom 71 were treated with artificial ventilation. An impressive change in the survival rates, 70% as compared with 23% in previous years, was seen. A survival rate of 50% in 8 ventilated babies with birthweights between 1,000 and 1,500gm is higher than any reported hitherto. The babies ventilated in 1971 were lighter, less mature, and more often asphyxiated at birth than in 1969 and 1970, yet there was an increased survival rate in 1971. The use of volume controlled respirators and the application of positive end-expiratory pressure and continuous positive airway pressure seem to have been major factors influencing the achieved improvement. The results in survival rate have been confirmed by a further analysis in patients treated in 1972. (19 refs.) - *A. C. Schenker.*

*University of Zurich
8006 Zurich, Switzerland

2404 **FITZHARDINGE, P. M.; & STEVEN, E. M.** The small-for-date infant. II. Neurological and intellectual sequelae. *Pediatrics,* 50(1):50-57, 1972.

A prospective follow-up study for a minimum of 5 years of 96 children (39 boys and 57 girls) with a severe degree of intrauterine growth retardation showed major neurological defects to be uncommon, whereas minimal cerebral dysfunction and EEG abnormalities were frequent. There was a strikingly low prevalence rate of cerebral palsy (1%), and convulsions occurred in only 6%, males being more affected than females. In contrast, there was a markedly high (25%) incidence of minimal brain dysfunction, and 59% of the boys and 69% of the girls suffered from EEG abnormalities, primarily of a diffuse mild nature. Speech defects involving immaturity of reception and expression were common, affecting 33% of the boys and 26% of the girls. Despite average IQs of 95 for the boys and 101 for the girls, only 11 of 22 boys and 16 of 25 girls were performing satisfactorily in school. No correlation was found between neurological and intellectual defects and the degree of intrauterine growth retardation, and later growth retardation and intellectual defects did not seem to be related except in cases of severe

MR, which was more prevalent among the males. (15 refs.) - *B. J. Grylack.*

McGill University
Montreal, Quebec, Canada

2405 **RIGATTO, HENRIQUE; & BRADY, JUNE P.** Periodic breathing and apnea in preterm infants. I. Evidence for hypoventilation possibly due to central respiratory depression. *Pediatrics,* 50(2):202-218, 1972.

Eighty-four studies were conducted with 20 "healthy" preterm infants during the first 34 days of life to determine whether preterm infants breathing periodically hypoventilate possibly as a result of central respiratory depression rather than because of a defect at the peripheral chemoreceptor level. Preterm infants breathing periodically when compared with those breathing regularly (1) hypoventilated, (2) showed a significant shift of the CO_2 response curve to the right with a 22% decrease in slope, (3) had an increase response to O_2, and (4) had similar alveolar-capillary Po_2 and Pco_2 differences. These findings suggested that the major defect was at the respiratory center (or central chemoreceptors). Babies breathing periodically during all or part of the first month of life behaved similarly, but they differed from babies breathing regularly. Hypoventilation was more striking when the duration of breathing/duration of apnea was low and was due mainly to decreased respiratory frequency with inadequate increase in tidal volume. Heart rate did not usually change with periodic breathing. The finding of a 16% decrease in ventilation in the regular breathing group as opposed to a 38% decrease in the periodic group suggested that the peripheral chemoreceptors are intact and hyperactive in babies breathing periodically. (41 refs.) - *B. J. Grylack.*

School of Medicine
University of Rio Grande Do Sul
Porto Alegre, Brazil

2406 **FANAROFF, AVROY A.; WALD, MICHAEL; GRUBER, HOWARD S.; & KLAUS, MARSHALL H.** Insensible water loss in low birth weight infants. *Pediatrics,* 50(2):236-245, 1972.

One hundred and thirty-three determinations of insensible water loss (IWL) were made on 30 immature and 9 small-for-gestational age, low birthweight infants by the technique of multiple weighings, beginning after the first day of life. Ten appropriately sized infants, all with birthweights below 1,250g and gestational ages less than 230 days, had IWL greater than 2.5g/kg/hr (equivalent to 60-120ml/kg/day), losses larger than previously reported, when studied under standard nursery conditions (infant nude, gavage feeding, and single-walled incubator). Significant reductions in IWL were seen when 6 of these infants were retested within the plastic heat shield ($p<.001$), in association with a significant rise in operative temperature and abdominal skin temperature ($p<.001$ and $p<.01$, respectively). The effect of the heat shield in reducing IWL in small premature infants appears to be a complex interaction of changing metabolic rate and altered physical environment. (32 refs.) - *B. J. Grylack.*

Babies' and Children's Hospital
Cleveland, Ohio 44106

2407 **LIGGINS, G. C.; & HOWIE, R. N.** A controlled trial of antepartum glucocorticoid treatment for prevention of the respiratory distress syndrome in premature infants. *Pediatrics,* 50(4):515-525, 1972.

The results of a controlled trial of betamethasone therapy administered to 282 mothers hospitalized during a 22-month period in premature labor at 24 to 36 weeks or in whom premature delivery before 37 weeks was planned because of an obstetrical complication support the hypothesis that glucocorticoid administration to the fetus accelerates lung maturation in the human, as has been shown previously in experimental animals. Among the 226 infants delivered of the 213 mothers in the unplanned premature labor group, there was a significantly lower perinatal death rate in the treatment group (6.4%) than in the controls (18.0%), due to a significantly lower early neonatal death rate in the former group (3.2% as compared with 15.0% of controls, p 0.01). Hyaline membrane disease was present at autopsy in 5 control infants but in none of the 93 betamethasone-treated liveborn babies, a difference probably significant at p 0.04. Intraventricular hemorrhage was present in 4 control infants but no treated infants. Respiratory distress syndrome was seen significantly less frequently in treated liveborn infants than in controls (4.3% as compared

with 24.0%, p 0.002), but the difference was limited to infants delivered at less than 32 weeks' gestation (11.8% as compared with 69.6%, p 0.02). Among infants under 30 weeks' gestation, 8 of 12 treated infants survived 28 days as compared with none of 8 controls, a probably significant difference. No complication of pregnancy, labor, delivery, or the puerperium was detected that could be attributed to steroid medication. (30 refs.) - *B. J. Grylack.*

National Women's Hospital
Auckland 3, New Zealand

2408 BADEN, MELVIN; BAUER, CHARLES R.; COLLE, ELEANOR; KLEIN, GEORGE; TAEUSCH, H. WILLIAM, JR.; & STERN, LEO. A controlled trial of hydrocortisone therapy in infants with respiratory distress syndrome. *Pediatrics,* 50(4):526-534, 1972.

A controlled study undertaken to assess the ability of postnatally administered hydrocortisone, as compared with a lactose placebo, to alter the course or outcome in 44 infants with respiratory distress syndrome did not indicate any clear advantage in either the course of respiratory distress syndrome or the final outcome for the hydrocortisone-treated infants as opposed to the controls. Even if administered early in the course of the disease, postnatal corticosteroids would appear to be ineffective as a therapeutic agent. The study did not reveal any significant effect of treatment upon PaO_2, $PaCo_2$ $[H^+]$, percent ambient oxygen needed, $A\text{-}aDO_2$ gradients, the need for assisted ventilation, or survival. During a 72-hour period following injection of either hydrocortisone or placebo, mean plasma corticosteroid values showed striking differences which persisted throughout the period. (28 refs.) - *B. J. Grylack.*

Brooke General Hospital
San Antonio, Texas

2409 NAVARRO, C.; & *MARTIN, J. J. Particularites lesionnelles dans l'ataxie-telangiectasie de Louis-Bar: dysmorphies nucleocytoplasmiques au niveau de la glie neuro-ganglionnaire et d'un certain nombre d'organes visceraux (Lesion peculiarities in Louis-Bar ataxia telangiectasia: nucleocytoplasmic dysmorphisms of the neuroganglionic glia and of a certain number of visceral organs). *Journal of the Neurological Sciences,* 17(2):219-231, 1972.

A new observation of ataxia telangiectasia (A-T) is described with particular attention focused on the vegetative and peripheral nervous system as well as on the particular characteristics of the glial and vascular lesions. An examination of the viscera revealed the classical A-T lesions such as generalized hypoplasia of the lymphatic system but associated with lymphosarcoma in one case; 2 other siblings who had been autopsied did not show the latter lesion. In the nervous system there were, besides the usual lesions, other alterations which were rare: together with the cerebellar cortical atrophy and posterior cordonal demyelinization, there was a deterioration of the spinal anterior horn cells and an involvement of the bulbar olives and of the dentate nuclei. Nucleocytoplasmic and nuclear anomalies were seen in the satellite cells of the spinal and sympathetic ganglia, as were Schwann cells, pituicytes, and some astrocytes situated in the marrow. Typical telangiectases were rarely seen in the nervous system. Examination by electron microscopy and immunological and virological research are urged in this field. (24 refs.) - *A. C. Schenker.*

*Fondation Born-Bunge
Berchem-Antwerp, Belgium

2410 LEROY, JULES G.; VAN ELSEN, AUGUST F.; MARTIN, JEAN-JACQUES; DUMON, JAN E.; HULET, ANDRE E.; OKADA, SHINTARO; & NAVARRO, CARMEN. Infantile metachromatic leukodystrophy: confirmation of a prenatal diagnosis. *New England Journal of Medicine,* 288(26):1365-1369, 1973.

The *in utero* diagnosis of metachromatic leukodystrophy is reported and its antenatal aspects described. The pregnant mother of a previous child who had died at the age of 5½ years from metachromatic leukodystrophy applied for an abortion during the fifth month of her fourth pregnancy. Amniotic fluid, obtained by amniocentesis, was shown to lack arylsulfatase A in the cultured fluid cells. The pregnancy was terminated and fetal tissue specimens were examined. In the amniotic fluid cells, arylsulfatase A activity was 7% of the average activity found in control strains;

this enzyme was virtually inactive in postmortem specimens of liver or brain and deficient in the fetal skin fibroblasts. The important conditions to observe in the prenatal diagnosis of a monogenically inherited disorder are: that the implicated enzymatic reaction must be detectable in the cultured amniotic cells obtained from control pregnancies; that the homozygous mutant genotype must be discernible from the heterozygous one in the cultured amniotic fluid cells; and that all recognized variables related to obtaining, propagating, and evaluating the amniotic cell cultures must be rigidly controlled. Any future therapeutic approach must take into account the antenatal aspects of the disorder. (29 refs.) - *A. C. Schenker.*

The Born-Bunge Institute
Antwerp, Belgium

MEDICAL ASPECTS—Convulsive Disorders

2411 **SPEIDEL, B. D.; & MEADOW, S. R.** Maternal epilepsy and abnormalities of the fetus and newborn. *Lancet*, 2(7782):839-453, 1972.

A retrospective survey was conducted on the outcome of 427 pregnancies in 186 epileptic women as compared with 483 pregnancies in 180 control women. There were 365 pregnancies among 168 epileptic women taking anticonvulsant drugs and 62 pregnancies among 27 epileptic mothers not taking these drugs. Seventeen babies with major congenital malformations were born to 16 epileptic mothers, all of whom had taken anticonvulsants during their pregnancies. This risk appeared to be 2 to 3 times greater than normal. There were only 7 malformed children in the control group. Four children born to epileptic mothers had multiple malformations. Congenital heart disease, cleft lip with or without cleft palate, and microcephaly were predominant among children born to epileptics. Of 23 children with malformations and other abnormalities born to epileptics, 6 were MR, 4 of them being SMR. Spontaneous hemorrhage occurred in 6 babies born to epileptics, 5 of whom took anticonvulsants throughout pregnancy. All perinatal deaths occurred in babies whose mothers took anticonvulsants during pregnancy; for this group the perinatal mortality rate was 42.5 per 1,000, as compared with 24.5 for controls. An increased incidence may be due to a combination of hereditary factors and the environmental insults of convulsions and their treatment. (21 refs.) - *B. J. Grylack.*

Southmead Hospital
Bristol, England

2412 **REYNOLDS, EDWARD H.; MATTSON, RICHARD H.; & GALLAGHER, BRIAN B.** Relationships between serum and cerebrospinal fluid anticonvulsant drug and folic acid concentrations in epileptic patients. *Neurology*, 22(8):841-844, 1972.

Forty-nine adult patients from seizure clinics and 23 control Ss were investigated for folic acid and anticonvulsant determinations in cerebrospinal fluid and blood serum. The ratio of serum to cerebrospinal fluid concentrations was found to be 8 to 1 for diphenylhydantoin, 2 to 1 for phenobarbital, and 1 to 1 for primidone. When serum phenobarbital was derived from oxidation of primidone in the 12 patients not otherwise receiving phenobarbital, the mean cerebrospinal fluid concentration was a third of that in the serum, irrespective of absolute serum phenobarbital concentration. Previous reports of a significant decrease of folic acid in serum in patients receiving anticonvulsants were confirmed. A highly significant decrease in spinal fluid folate was also found in comparison with the control group. The findings suggested that diphenylhydantoin has a more significant effect on folate concentrations than phenobarbital and that the fall in serum and fluid folate is partially a function of the diphenylhydantoin concentration. This relationship is not always seen, however. (22 refs.) - *B. J. Grylack.*

Institute of Psychiatry
Denmark Hill
London, S.E. 5, England

2413 **SOLOMON, GAIL E.; HILGARTNER, MARGARET W.; & KUTT, HENN.** Coagulation defects caused by diphenylhydantoin. *Neurology*, 22(11):1165-1171, 1972.

Experiments were conducted to determine whether diphenylhydantoin could induce clotting deficiencies *in vivo* using adult cats, and in *vitro* using rat liver slices, and pregnant cats and their kittens were studied for the transplacental transfer of diphenylhydantoin as well as the effect of the drug on vitamin-K dependent clotting factors in the neonatal kittens. Assays with pregnant cats and their offspring showed that diphenylhydantoin alone can depress vitamin K-dependent factors. The drug was found to reduce these factors in adult cats in relation to dose, the cats on the highest dosage showing the most marked reduction of the vitamin K-dependent factors and now showing recovery to normal levels, and animals receiving both diphenylhydantoin and vitamin K demonstrating the ability of the vitamin to protect against clotting defects in cats. The mechanism by which diphenylhydantoin affects coagulation may be similar to that of warfarin. The significance of these findings is applicable to the newborn infant. Administration of vitamin K may prevent the clinical signs of bleeding seen in some infants as a result of maternally transferred diphenylhydantoin and subsequent depression of clotting factors in the infants. (15 refs.) - *B. J. Grylack.*

New York Hospital-Cornell Medical Center
New York, New York 10021

2414 **GALLAGHER, BRIAN B.; BAUMEL, IRWIN P.; & MATTSON, RICHARD H.** Metabolic disposition of primidone and its metabolites in epileptic subjects after single and repeated administration. *Neurology*, 22(11):1186-1192, 1972.

The absorption and subsequent disposal of primidone after single or multiple dosing were investigated in 26 adult epileptic patients with grand mal and/or temporal-limbic disorders. In contrast to phenobarbital, primidone was shown to be eliminated from the body relatively rapidly. The average 8-hour half-life found in these patients was slightly less than the corresponding value reported for normal Ss. Primidone metabolism might well be altered during chronic exposure to the drug in some individuals. Study of the disappearance of primidone and its metabolites from plasma in 2 Ss during acute withdrawal of primidone after they had been receiving the drug chronically for more than 2 years indicated clearance rates roughly proportional for primidone, phenylethylmalonamide, and phenobarbital within each individual, although the second S required approximately twice as long to clear the drug and its metabolites. The formulation and accumulation of phenylethylmalonamide and phenobarbital from primidone *in vivo* appeared to be a function of a complex set of conditions. (8 refs.) - *B. J. Grylack.*

Yale University School of Medicine
New Haven, Connecticut 06510

2415 **HAERER, ARMIN F.; & BUCHANAN, ROBERT A.** Effectiveness of single daily doses of diphenylhydantoin. *Neurology*, 22(10):1021-1025, 1972.

Single daily doses of diphenylhydantoin to 13 epileptic patients under controlled conditions did not produce any evidence of increased clinical toxicity, and plasma concentrations were found to be remarkably uniform from the time of peak absorption to just prior to the next dose. Once-daily administration of diphenylhydantoin to epileptics could offer a convenience for the active school-age patient or busily employed adult and could reduce the motivational problem associated with the taking of medication. The single daily schedule should not be used for other anticonvulsants, such as primidone, which have a much shorter biologic half-life. (13 refs.) - *B. J. Grylack.*

University of Mississippi
Medical Center
Jackson, Mississippi

2416 **FROMM, GERHARD H.; & KOHLI, CHANDER M.** The role of inhibitory pathways in petit mal epilepsy. *Neurology*, 22(10):1012-1020, 1972.

Examination of the effect of Tridione and Zarontin on corticofugal inhibition of afferent activity in the spinal trigeminal nucleus of 41 adult cats weighing 2.2 to 3.5kg supported the hypothesis that Tridione significantly decreases this inhibition. An increase in the latency of response of some trigeminal nucleus neurons to maxillary nerve stimulation by 0.3 to 3.6msec, when a conditioning stimulus was applied to the contralateral coronal gyrus 100msec before the test stimulus to the maxillary nerve, was reduced temporarily by injecting 10mg/kg of Tridione. Administration of 20 and 40mg/kg had increasingly prolonged effects. The magnitude of the

effect produced by Tridione depended primarily upon the amount of corticofugal inhibition that could be demonstrated in control records. When injected in a dose of 10 to 25mg/kg, Zarontin resembled Tridione in its ability to depress cortical inhibitory pathways, but administration of 5mg/kg of Dilantin or 6mg/kg of Tegretol further increased the latency of response of the trigeminal nucleus neurons to maxillary nerve stimulation following a conditioning stimulus to the contralateral coronal gyrus and to maxillary nerve stimulation alone. The results suggested that petit mal spells represent paroxysmal activity in cortical inhibitory pathways. (37 refs.) - *B. J. Grylack.*

University of Pittsburgh School
of Medicine
Pittsburgh, Pennsylvania 15213

2417 **SPRAY, G. H.; & BURNS, D. G.** Folate deficiency and anticonvulsant drugs. *British Medical Journal*, 2(5806):167-168, 1972. (Letter)

Estimation of glutamate forminotransferase and methylene tetrahydrofolate dehydrogenase, as well as serum and liver folates, in immature male or female Wistar albino rats fed on or injected with phenobarbitone, diphenylhydantoin, or a combination indicated a general increase in the activity of both enzymes. In most cases there were significantly increased activities of both enzymes in the liver, but there were usually no significant differences in folate levels. The results support the previous suggestion that the folate deficiency occurring after administration of anticonvulsant drugs may be due to hepatic enzyme induction. (5 refs.) - *B. J. Grylack.*

Nuffield Department of Clinical
Medicine
Radcliffe Infirmary
Oxford, England

2418 **LEFEBVRE, ELIZABETH BORRONE; HAINING, ROBERT C; & LABBE, ROBERT F.** Coarse facies, calvarial thickening, and hyperphosphatasia associated with long-term anticonvulsant therapy. *New England Journal of Medicine*, 286(24):1301-1302, 1972.

One-third of 222 MR patients with seizures were found to have gross enlargement of the lips, nose, and thickening of the facial and scalp subcutaneous tissues, while the others were either unaffected or marginally affected. Twenty-nine with extensive facial changes were compared to 23 with convulsive disorders but no facial changes. Diphenylhydantoin was often administered in combination with phenobarbitol, primadone, diazepam, or ethosuxamide to both groups for seizure control. Of those with facial changes, 72% had more than 1 seizure per mo, 62% received 3 or more drugs, 62% had serum drug levels above therapeutic norms, and most were lethargic. Among those without facial change, 1 had more than 1 seizure per mo, 83% received only 1 or 2 anticonvulsants, 22% had high serum drug levels, and all were more active. Gingivectomies were required in 69 and 13% of the facial change and nonfacial change groups, respectively. Mean alkaline phosphatase activities were 174 mU/ml and 108 mU6ml in the two groups, respectively (vs normal value of 30-85 mU/ml). The changes may be due to prolonged administration of anticonvulsant drugs. The somnolence-producing doses of drug necessary to elicit the FC would probably be tolerated by inst MR, but not by mentally active people, which explains the restriction of the syndrome to inst populations. (9 refs.) - *V. J. Goldberg.*

University of Washington
Seattle, Washington 98195

2419 **SMITH, DENNIS B.; & RACUSEN, LORRAINE C.** Folate metabolism and the anticonvulsant efficacy of phenobarbital. *Archives of Neurology*, 29(1):18-22, 1973.

The effects of long-term phenobarbital administration on plasma folate levels were studied in rats, to determine the relationship between plasma folate levels and anticonvulsant action, as well as that between chronic phenobarbital administration and vitamin B_{12} metabolism. The Ss were male Sprague-Dawley albino rats, studied in groups of 12 and 14 animals; fluorothyl was infused at 40 microl/min into an airtight plastic chamber where it volatilized. All animals were fed vitamin-free casein, and a vitamin fortification mixture was added to different groups. Phenobarbital was administered i.p. at 13 mg/ml to half the animals in each group. Seizures were induced in all animals every 1-2 weeks for 10 weeks. A significant folate deficiency was produced after 10 weeks in the animals on folate deficient diets, with no such

deficiency seen in animals on a normal control diet and in those treated with succinyl sulfathiazole. Animals receiving phenobarbital had lower plasma folate levels than controls, the decreases being most marked in those animals receiving a diet supplemented with folate and vitamin B_{12}. Phenobarbital raised the seizure threshold in all groups. The results suggest a relationship between folate metabolism and the anticonvulsant efficacy of phenobarbital in rats, but do not suggest any relationship between phenobarbital administration and vitamin B_{12} levels. (24 refs.) - *A. C. Schenker.*

Medical Center Hospital of Vermont
Burlington, Vermont 05401

2420 **SHERWIN, ALLAN L.; ROBB, J. PRESTON; & LECHTER, MORTIMER.** Improved control of epilepsy by monitoring plasma ethosuximide. *Archives of Neurology*, 28(3):178-181, 1973.

The clinical effectiveness of periodic monitoring of plasma ethosuximide levels in absence seizures was studied in 70 patients. Plasma ethosuximide levels were remarkably stable in individual patients receiving various amounts of medication consistently. This response was utilized to test the relationship between seizure control and adjusted plasma levels. Plasma ethosuximide levels were directly related to administered dose. Initial monitoring of plasma ethosuximide levels revealed that 38% of the uncontrolled patients had abnormally low dose-level responses, but following regular plasma monitoring, these patients achieved the same level-dose responses as the controlled group (and a reduction of seizures in 48%). This response is due to the fact that patients with epilepsy are prone to noncompliance with drug therapy. Compliance may be partial or erratic, with levels occasionally falling below individual therapeutic requirements in consistent failure to take medication, or excess consumption of drugs, which may lead to toxic effects. Regular monitoring of plasma ethosuximide levels improved the effectiveness of treatment of patients with absence seizures. (15 refs.) - *A. C. Schenker.*

Montreal Neurological Institute
Montreal 112, Canada

2421 **GASCON, GENEROSO; VICTOR, DAVID; LOMBROSO, CESARE T.; & GOODGLASS, HAROLD.** Language disorder, convulsive disorder, and electrocardiographic abnormalities. *Archives of Neurology*, 28(3):156-162, 1973.

An unusual disorder, consisting principally of an acquired language disorder of long duration, a self-limited convulsive disorder, and bilateral EEG abnormalities, is described in 2 children (age 7½ years) and in a 21-year-old man. The course of language loss suggests a subacute inflammatory process. The subacute progression is consistent with the time course of a slow virus disease, such as subacute sclerosing panencephalitis (SSPE). This entity often presents first with mental symptoms, often with apraxic difficulties, though thus far never with aphasia. Circumstantial evidence points to bilateral cortical or subcortical temporal lobe lesions, or both, in these patients. This is based on the hearing loss, the prolonged recovery from the aphasia, the global attentional disorder, and the EEG abnormalities. The 2 etiological possibilities are therefore: a focal encephalitis or a pathogenetic mechanism related to a convulsive disorder. (25 refs.) - *A. C. Schenker.*

Children's Hospital Medical Center
Boston, Massachusetts

2422 **SU, PHILIP C.; & FELDMAN, DANIEL S.** Motor nerve terminal and muscle membrane stabilization by diphenylhydantoin administration. *Archives of Neurology*, 28(6):376-379, 1973.

The effects of diphenylhydantoin (DPH) on neuromuscular synapse were investigated *in vivo* in rats, using an intracellular microelectrode. DPH was given i.v. in 5 rats at 40mg/kg (total 30 fibers observed). When DPH was given at various doses, there was a significant increase of membrane potential of about 15% to -45mV compared to the control group. Resting membrane potential was -72.6mV. Resting miniature endplate potential (mepp) was 2-4/sec in most fibers. When high potassium solution was used to depolarize the preparation, the mepps increased to 100/sec. This augmented mepp frequency was reduced when DPH was given, suggesting that there is a nerve membrane repolarization or membrane stabilization. The present observation that DPH stabilizes the excitable terminal nerve membrane suggests a mechanism for its effect in nerve terminal hyper-

activity and in the treatment of myotonia. (26 refs.) - *A. C. Schenker.*

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Columbia University
710 W 168th St.
New York, New York 10032

2423 **BRODERSEN, PAUL; PAULSON, OLAF B.; BOLWIG, TOM G.; ROGON, Z. EDWARD; RAFAELSEN, OLE J.; & LASSEN, NIELS A.** Cerebral hyperemia in electrically induced epileptic seizures. *Archives of Neurology*, 28(5):334-338, 1973.

Cerebral blood flow (CBF) and cerebral metabolic rate of oxygen were measured in anesthetized, paralyzed, and artificially ventilated men during electrically induced seizures, in order to determine whether lactacidosis occurs when arterial normoxemia is preserved during and after seizure. The Ss were 11 patients with endogenous depression who were receiving electroconvulsive therapy (ECT). CBF was measured using injection of xenon Xe 133 into the internal carotid artery and external washout. CBF, oxygen, and glucose uptake doubled during seizures. The jugular venous oxygen and CO_2 tensions increased markedly within 1 min of the ECT. The inconstancy of the arterial lactate concentration and the finding of a V-A lactate concentration of 0.22 millimol/liter in the resting state indicate an unsteady state; thus such measurements are not ideal for detecting short increases in brain lactic acid production. A-V differences for both CO_2 and O_2 changed rapidly during and after seizures, resulting in biphasic RQ changes. The mechanism by which CBF increases during seizures most likely involves both a rise in arterial blood pressure and a metabolic acidosis causing impaired autoregulation and vasodilatation. (23 refs.) - *A. C. Schenker.*

Bispebjerg Hospital
DK-2400 Copenhagen NV Denmark

2424 **BOCHNER, F.; HOOPER, W. D.; TYRER, J. H.; & EADIE, M. J.** Factors involved in an outbreak of phenytoin intoxication. *Journal of the Neurological Sciences*, 16(4):481-487, 1972.

The outbreak of an anticonvulsant intoxication in epileptic patients treated with phenytoin, and the conclusion that the excipient might be responsible for this toxicity, prompted a study of the effects of a change in excipients upon the blood phenytoin concentration. The Ss were 13 chronic neurological patients who were receiving phenytoin for major epilepsy. It was revealed that only calcium sulfate significantly ($p<0.01$) altered blood phenytoin concentrations. The data were consistent with the view that phenytoin absorption from the gut was reduced when phenytoin capsules containing calcium sulfate excipient were taken; that the reduced amount of phenytoin absorbed into the body was responsible for the fall in plasma phenytoin concentration; and that the decreased urinary excretion of phenytoin and decreased urinary and fecal loss of phenytoin metabolite were secondary to phenytoin absorption. The phenytoin intoxication in Australia occurred when the excipient containing calcium sulfate was changed to the lactose excipient; the absorption rate rose and the concentration in the blood thus reached toxic levels. (8 refs.) - *A. C. Schenker.*

University of Queensland
Royal Brisbane Hospital
Brisbane, Australia

2425 **EWEN, LILLIAN M.; & GRIFFITHS, JOHN.** Gamma-glutamyl transpeptidase: elevated activities in certain neurologic diseases. *American Journal of Clinical Pathology*, 59(1):2-9, 1973.

Elevations of serum γ-glutamyl transpeptidase are described in patients with epilepsy and in some patients with intracranial tumors. The study included 142 patients, 75 with epilepsy, 33 with multiple sclerosis, 11 with Parkinson's disease, and 23 with intracranial tumors. The conclusions drawn from the study were that serum-γ-glutamyl transpeptidase, which is elevated in epileptic patients, does not result from hepatoxicity of the drug administration. γ-glutamyl transpeptidase may be elevated preoperatively in the sera of some patients with brain tumors and postoperatively; this enzyme may follow a pattern similar to that following myocardial infarction. In these cases peak activity is seen in the second week after tissue insult. The postulated function of γ-glutamyl transpeptidase in the transfer of amino acids across cellular membranes and the importance of glutamate in cerebral metabolism lead to speculation about a function of the enzyme in

provision of glutamate to tissues. (26 refs.) - *A. C. Schenker.*

Vancouver General Hospital
Vancouver, Canada

2426 **HOMMES, O. R.; & OBBENS, A.M.T.** The epileptogenic action of Na-folate in the rat. *Journal of the Neurological Sciences*, 16(3):271-281, 1972.

The finding of a strong convulsive action of sodium folate (Na-folate) in normal and epileptic rats is reported. The experimental Ss were young female Wistar rats with implanted electrodes for electrocorticography (ECoG). In normal rats, i.v. injections of 15-45mg Na-folate did not change the EEG. Doses between 60 and 90mg produced epileptic discharges between 20 and 75 minutes after injection. To produce focal epileptic activity, a metallic cobalt rod was implanted in the right sensorimotor cortex. In rats with ECoG, i.v. injections produced epileptic discharges with a dose of 15mg. In cobalt-epileptic rats, the epileptogenic effect of Na-folate produced activation of focal discharges 10-40 seconds after injection by doses of 0.05 and 0.01mg; 0.5 microgram close to the cobalt rod produced activation of the epileptic focus. A clear difference is seen between the effects of Na-folate in rats without and rats with brain lesions, as recorded by implanted electrodes. It is possible that the blood-brain barrier cannot be penetrated by Na-folate except in high doses. (16 refs.) - *A. C. Schenker.*

Radboud University Hospital
Nijmegen, The Netherlands

2427 **GORDON, NEIL.** Clinics for the treatment of epilepsy and convulsions. *Lancet*, 1(7763):1285-1286, 1972. (Letter)

Special clinics for epileptic patients have long been a subject of controversy. While there is general agreement as to the need for long-term treatment and management clinics, comprehensive diagnostic centers for epileptic patients have seemed impractical because of the many possible etiological factors involved. Much of the opposition to special treatment and management epileptic clinics, which are urgently needed, would disappear if the diagnostic center concept were treated as a separate question. - *N. Mize.*

Royal Manchester Children's Hospital
Pendlebury, near Manchester M27 1HA
England

2428 **BROWN, J. K.; COCKBURN, F.; & FORFAR, J. O.** Clinical and chemical correlates in convulsions of the newborn. *Lancet*, 1(7742): 135-138, 1972.

Over a 2-year period 142 infants with neonatal convulsions were examined neurologically and biochemically, and the survivors were reexamined at 4 mos and at 1 yr of age. Neonatal seizures, generally, carry an adverse prognosis and by the end of the first year, 39% of the group had died or were obviously handicapped. Onset of convulsions was of prognostic and diagnostic significance, with convulsions due to brain damage tending to occur during the first 3 days of life or after the eighth and convulsions attributable to metabolic disturbances between the fifth and eighth days. The frequency of death and severe handicap was 4 and 6 times as great in the 62 infants categorized as cases of brain damage. This significant difference in prognosis makes it important to distinguish between the two conditions, as therapeutic measures will differ. More useful than blood biochemistry in making this distinction are certain neurological and behavioral signs, including time of onset of convulsion, specific evidence of neurologic disease, associated clinical features, and type of convulsion. (15 refs.) - *N. Mize.*

*Royal Hospital for Sick Children
Edinburgh, Scotland

2429 **LEVINE, MARK C.** Reactions to anticonvulsants. *New England Journal of Medicine*, 286(22): 1217, 1972. (Letter)

Leukopenia as a side effect of acetazolamide, ethosuximide, and methsuximide is sufficiently rare that the additional expense and trauma to the patient of white cell counts and urinalysis are probably unjustifiable. - *V. J. Goldberg.*

2430 **TEOTIA, MOHINI; & TEOTIA, SURENDRA P. S.** Rickets precipitated by anticonvulsant drugs in a child receiving prophylactic vitamin D. *American Journal of*

Diseases of Children, 125(6):850-852, 1973.

A relapse of rickets, while receiving anticonvulsant therapy, is reported in a 14-year-old girl who was receiving phenobarbital for epilepsy. The nutritional lack of vitamin D and calcium in the diet and the response to small doses of ergocalciferol confirmed the initial diagnosis of privational rickets. The return of symptoms 9 months later in spite of an adequate diet and prophylactic administration of ergocalciferol suggested the role of anticonvulsant therapy in the relapse, particularly with the addition of diphenylhydantoin to the therapy. It appears that the anticonvulsant drugs increased the requirement for vitamin D. (10 refs.) - *A. C. Schenker*.

LLRM Medical College
Meerut, India

2431 **REYNOLDS, E. H.** Anticonvulsants, folic acid, and epilepsy. *Lancet*, 1(7816):1376-1378, 1973.

Recent clinical and experimental observations have given support to the hypothesis that the antiepileptic action of the 3 major anticonvulsants may be mediated, if only partially, by their antifolate action. The evidence has indicated that diphenylhydantoin, phenobarbitone, and primidone all affect serum-folate levels in most patients, that cerebrospinal fluid folate was also lowered by these drugs, and that treatment with folic acid could reverse the clinical effects of the drugs in many patients. With a considerable blood/brain barrier to the uptake of the vitamin existing, however, most of the folic acid that is administered orally or parenterally will accumulate in other tissue or be excreted, with the dose and duration of therapy determining the effect of the limited amount that does enter the nervous system. The fact that folic acid and its derivatives are convulsants strengthens the hypothesis of a relationship between antiepileptic and antifolate mechanisms and has broad implications for new possibilities of studying biochemical processes underlying seizure mechanisms. (61 refs.) - *B. J. Grylack*.

Institute of Psychiatry
De Crespigny Park
London S.E. 5, England

2432 **JEAVONS, P. M.** Special handicaps: epilepsy. In: Griffiths, Margaret I., ed. *The Young Retarded Child: Medical Aspects of Care*. Baltimore, Maryland, Williams & Wilkins, 1973, Chapter 13, p. 145-153.

Epilepsy and subnormality are common symptoms of cerebral disease and are frequently associated. Around 25% of MR persons are afflicted with varying degrees of epilepsy. The appearance of epilepsy in infancy is variable and may include tonic, bilateral clonic, and focal fits. Neonatal fits are commonly associated with perinatal insult, biochemical disorders, meningitis, or pyridoxine deficiency. Fits occurring after the neonatal period may indicate cerebral agenesis, cortical malformations, inborn errors of metabolism, heredofamilial and degenerative diseases, cerebral infections, or toxins. Infantile spasms are of 3 types: flexor, extensor, and lightning. Febrile convulsions may occur without subsequent development of epilepsy. Myoclonus and myoclonic epilepsy present the greatest difficulty in classification. Other types include myoclonic-astatic petit mal, grand mal, true petit mal, and photosensitive epilepsy. Therapy for epilepsy includes anticonvulsant drugs and limited environmental controls for certain types. - *C. Wares*.

University of Birmingham
Birmingham, England

2433 **KUENSSBERG, E. V.; & KNOX, J.D.E.** Teratogenic effect of anticonvulsants. *Lancet*, 1(7796):198, 1973. (Letter)

Preliminary results of a study in Scotland on the incidence of cleft palate in the children of epileptic mothers on drugs are submitted in connection with Dr. South's suggestion of such an association. In this study of 15,181 outcomes (including abortions), there were 452 malformations, 30 of which were cleft lip and/or palate; none of the latter was associated with an epileptic mother, either having anticonvulsant therapy or not. Of 48 epileptic mothers, 43 had normal outcomes; there were 1 hydrocephalus, 2 minor anomalies, and 2 doubtful abnormalities. It is submitted that the evidence for a causative relationship between anticonvulsant therapy and congenital abnormality is insufficient to cause any alteration to the current practice of continuing therapy throughout pregnancy in a known epileptic mother, or to

terminate pregnancy on this basis. (2 refs.) - *A. C. Schenker.*

University of Dundee
166 Nethergate
Dundee DD1 4DR, United Kingdom

2434 MILLAR, J.H.D.; & NEVIN, N. C. Congenital malformations and anticonvulsant drugs. *Lancet*, 1(7798):328, 1973. (Letter)

Congenital malformations in infants born to epileptic mothers have been reported by several authors; a study of 110 births to 57 epileptic women taking anticonvulsants throughout pregnancy is added to these data. Of the 110, 7 infants were born with malformations; their mothers had taken anticonvulsants during the first trimester. This rate, 6.4% of malformations, is compared with a malformation-rate of 3.8% for all live and still births in Northern Ireland. The incidence of cleft lip with or without cleft palate among infants of epileptic mothers was 1.8% compared with 0.22% among all infants. Only 1 infant of an epileptic mother had a neural-tube defect. It is submitted that anticonvulsant therapy is necessary during pregnancy and the risk of an abnormal baby to a mother with epilepsy is small. - *A. C. Schenker.*

Royal Victoria Hospital
Belfast BT12 6BA, Northern Ireland

2435 TARTER, RALPH E. Intellectual and adaptive functioning in epilepsy. A review of 50 years of research. *Diseases of the Nervous System*, 33(12):763-777, 1972.

Critical examination of the variables that influence intellectual and adaptive functioning in epilepsy, as studied during the last half century, has revealed important determinants of intellectual deterioration and several interesting findings regarding the relationship between EEG patterns and intellectual functioning. The higher the IQ of the premorbid epileptic, the greater is the degree of deterioration. With the exception of petit mal epilepsy, IQ is negatively correlated with the total number of seizures. The earlier the onset of convulsions and the longer the duration of the disease, the lower is the adult IQ. There is greater propensity for a seizure discharge during passivity than during psychological testing. Slow wave EEG activity appears to be the most detrimental to intellectual efficiency. From a neuropsychological perspective, it has been found that the epileptic focus corresponds to the particular type of psychological impairment. (43 refs.) - *B. J. Grylack.*

Carrier Clinic Foundation
Belle Mead, New Jersey 08502

2436 CHIEN, CHING-PIAO; & KEEGAN, DAVID. Diazepam as an oral long-term anticonvulsant for epileptic mental patients. *Diseases of the Nervous System*, 33(2):100-104, 1972.

Of 42 mental patients with past histories of repeated grand mal seizures and with resultant long-term anticonvulsant therapy, 22 patients continuing on their previous medication, primarily Dilantin and phenobarbital, were compared with 20 patients who were taken off their former anticonvulsant medication and started immediately on diazepam. Each group received the given medication for a 6-month period. While the number of patients experiencing seizures and the total number of seizures among the 2 groups remained almost equal, the type or severity of seizure differed significantly ($p<0.05$), the diazepam group having a significantly higher number of grand mal seizures and the standard treatment group a higher incidence of minor seizures. In both groups, the patients with seizures received higher dosages than their nonseizure counterparts. Evaluation of patients' mental status by the Nurses Observation Scale for Inpatient Evaluation indicated, surprisingly, that those on standard anticonvulsants generally did better than those on diazepam, especially in regard to behavioral control of psychotic symptoms. (20 refs.) - *B. J. Grylack.*

Boston State Hospital
Boston, Massachusetts

2437 BUCHANAN, ROBERT A.; KINKEL, ARLYN W.; GOULET, J. RICHARD; & SMITH, THOMAS C. The metabolism of diphenylhydantoin (Dilantin) following once-daily administration. *Neurology*, 22(2):126-130, 1972.

Plasma levels, metabolic disposition, and possible side effects resulting from a once-daily dose of

diphenylhydantoin (Dilantin) were compared with those from the same dose divided 3 times daily in 24 normal adult male volunteers. Ss were confined to the clinic throughout the study. Both the single- and the divided-dose schedule demonstrated similar rates of absorption and equilibrium levels, steady state being achieved 7-8 days after initiation of medication. After cessation of drug administration (300mg daily or 200mg x 3), the mean biologic half-life was 27.91hr for the single-dose group and 30.03hr for the divided-dose group. After attaining steady state, the mean plasma level was 8.23 microgm/ml for the single-dose and 8.83 microgm/ml for the divided-dose groups. More episodes of nystagmus were recorded for the single-dose group than for the divided-dose group. No particular correlation between blood levels and nystagmus could be detected. Once-daily administration of Dilantin is more convenient for the patient, and single administration also reduces the time expenditure in inst. The frequency of nystagmus in the single dose group was considered to be overinterpreted and not a serious consideration in judging the mode of administration. (13 refs.) - *A. C. Schenker.*

Parke, Davis & Co.
Ann Arbor, Michigan 48106

2438 **RABE, EDWARD F.** Anticonvulsant therapy: to stop or not to stop. *New England Journal of Medicine*, 286(4):213-214, 1972.

Management of childhood epilepsy is discussed from the viewpoint of the choice of the initial anticonvulsant and the maintenance of the child in remission, and the length of time that treatment must be continued. The physician must choose from among a group of drugs that present knowledge indicates to be most likely to stop the seizures. The drug dosage must be based on body weight or surface area; if, in spite of the calculated dosage on this basis, the response is inadequate, serum drug levels should be determined to help drug control. The most important factor in arriving at a state of remission is the length of the follow-up period. Discontinuation of medication after 4 years of remission is considered safe; the medication should be discontinued gradually. In the case of petit mal seizures treated with a specific "anti-petit mal" drug, some authors found continued seizure remissions when drug therapy was stopped. Factors affecting this course were: onset of seizures before 8 years of age; early control of seizures; seizure type (grand-mal petit-mal, and simple febrile seizures had the lowest relapse type); and absence of neurologic or psychologic deficits. (6 refs.) - *A. C. Schenker.*

2439 **ARKY, RONALD A.** Diphenylhydantoin and the beta cell. *New England Journal of Medicine*, 286(7):371-372, 1972.

The suppression of the insulin response of the glucose stimulated beta cell by diphenylhydantoin and other drugs affecting the response of the beta cell is discussed in connection with patients who are in precarious metabolic balance. The administration of therapeutic doses of diphenylhydantoin to patients with maturity-onset diabetes may precipitate a hyperglycemic, nonketotic coma. Beta-adrenergic stimulation enhances, whereas alpha-adrenergic stimulation inhibits the secretion of insulin; therefore agents such as isoproterenol augment the release of insulin by the glucose stimulated beta-cell. Epinephrine has an inhibitory action and would be expected to aggravate the diabetic state. Theophylline ethylenediamine, used for treatment of cardiac or asthmatic patients, inhibits the activity of phosphodiesterase, augmenting the insulin response to a glucose challenge. Other agents affecting insulin release are some biogenic monoamines (serotonin), some benzothiadiazides, and other pharmacologic agents which influence extracellular concentration of calcium. (4 refs.) - *A. C. Schenker.*

2440 **HOLOWACH, JEAN; THURSTON, DON L.; O'LEARY, JAMES.** Prognosis in childhood epilepsy: follow-up study of 148 cases in which therapy had been suspended after prolonged anticonvulsant control. *New England Journal of Medicine*, 286(4):169-174, 1972.

The question as to whether to discontinue anticonvulsant therapy after prolonged seizure control prompted a follow-up study of 148 children for 5-12 years after discontinuation of therapy. Repeat EEG's were taken before medication was discontinued; drowsy and sleep sequences were observed. Where several drugs had been administered simultaneously, only one was discontinued at a time over a 9-month period. In all cases medication was resumed in the previous full dosage if seizures recurred during drug withdrawal.

The Ss comprised 67 girls and 81 boys; the rate of recurrence was 28% and 21%, respectively. A positive family history did not affect the recurrence. Children whose seizures began before 8 years of age had a rate of only 13% relapse upon discontinuation of drug. The highest recurrence rate was in patients 16-18 years old and the largest percentage of relapses was in the group of children with an intermediate degree of seizure severity. Gross psychologic or neurologic deficits were observed in 24% of the children. The EEG findings were not predictive of prognosis on suspension of treatment. The greatest risk in suspension of drugs was encountered in children whose epilepsy developed during puberty; patients with grand mal type seizures had the best prognosis and those with jacksonian ((53% relapse) or multiple seizures (40% relapse) had the worst prognosis. (10 refs.) - *A. C. Schenker.*

Washington University School
of Medicine
St. Louis, Missouri

2441 **MALHERBE, CHRISTIAN; BURRILL, KAREN C.; LEVIN, SEYMOUR R.; KARAM, JOHN H.; & FORSHAM, PETER H.** Effect of diphenylhydantoin on insulin secretion in man. *New England Journal of Medicine*, 286(7):339-342, 1972.

The effect of diphenylhydantoin (DPH) upon early and late phases of insulin release during intensive and sustained glucose stimulation in normal Ss is described. Six healthy men, aged 20-30 years, with no family history of diabetes were studied. All Ss consumed 200gm of carbohydrate daily for 3 days prior to study, and were tested fasting. A glucose priming load (0.33gm/kg) was given i.v. and followed by 20% glucose infusion during 148 min at a constant rate of 20mg/kg/min. Blood and urinary glucose levels were determined by a glucose oxidase method; serum insulin by the method of Grodsky and Forsham; serum DPH by gas chromotography; and serum protein binding of DPH by modification of the Lundemethod with ^{14}C-labeled DPH. In every S, serum insulin levels before and after DPH showed an early peak, followed by a late rise, characterized by a progressive and sustained increase in insulin levels until the end of the infusion. The administration of DPH significantly decreased the early insulin peak from a mean value of 130 ± 23 microU/ml to a mean value of 70 ± 12 microU/ml ($p<0.01$). DPH inhibits insulin responsiveness to glucose in normal young adults and should therefore be carefully monitored in patients with risk factors for diabetes. (27 refs.) - *A. C. Schenker.*

University of California
San Francisco, California

2442 **JEAVONS, P. M.** Clinics for the treatment of epilepsy and convulsions. *Lancet*, 2(7756):904, 1972. (Letter)

A survey of 276 adult patients seen at an epilepsy clinic and of 195 children seen at an interdisciplinary convulsions clinic indicated that 44% of adults and 63% of children had been seen previously by another consultant, 13% of adults and 10% of children had been referred to another consultant, and 19% of adults and 21% of children were not regarded as having epilepsy. Both clinics are open to new patients. The emphasis in a special epilepsy clinic should be on diagnosis as well as on follow-up. (1 ref.) - *B. J. Grylack.*

42 Westfield Road
Edgbaston
Birmingham B15 3QG, England

2443 **CHRISTIANSEN, CLAUS; KRISTENSEN, MOGENS; & RODBRO, PAUL,** Latent osteomalacia in epileptic patients on anticonvulsants. *British Medical Journal*, 3(5829):738-739, 1972.

Five male and 5 female epileptic patients (CA 21 to 57 years) on long-term treatment with phenytoin (mean 6.2 years) were measured for bone mineral content before and during treatment with vitamin D. Although the Ss did not show biochemical signs of osteomalacia, none of the 10 initial values were higher than the corresponding normal mean value, and 4 of the 10 were below the normal range. The mean bone mineral value rose significantly during treatment, a reaction suggesting the existence of latent osteomalacia. The findings suggested that this condition may exist in a fairly high proportion of epileptic patients taking anticonvulsants. (12 refs.) - *B. J. Grylack.*

Glostrup Hospital
2600 Glostrup, Denmark

2444 **LINDSAY, JANET.** The difficult epileptic child. *British Medical Journal*, 3(5821):283-285, 1972.

Children with seizures may show and create difficulties at all levels, the particular syndromes manifested by these children depending upon the type of seizure disorder, the premorbid personality of the child, the family psychopathology, and the effect of medical treatment on the child's handicap. Cataclysmic rage occurs in approximately one-third of children with temporal lobe epilepsy. Some children with seizure disorders are said to show distractibility with perseveration, and their education and training are particularly difficult when the behavior is intense. While considerable MR generally accompanies gross neuronal loss plus epilepsy, epilepsy may be compatible with high intellectual functioning. Underachievement at school is common among epileptic children, but both the IQ and learning capacity of these children may show appreciable fluctuation. Children with epilepsy are more prone than usual to neurotic or conduct disorders, but a psychotic breakdown before puberty in these individuals is rare. Careful and repeated assessments of the child and his surroundings will help to reduce secondary and tertiary handicaps. (2 refs.) - *B. J. Grylack.*

Park Hospital for Children
Oxford, England

2445 **STAMP, T.C.B.; ROUND, J. M.; ROWE, D.J.F.; & HADDAD, J. G.** Plasma levels and therapeutic effect of 25-hydroxycholecalciferol in epileptic patients taking anticonvulsant drugs. *British Medical Journal*, 4(5831):9-12, 1972.

Nineteen normal adults and 12 normal adolescent boys were compared with 11 epileptic adults on long-term high-dosage anticonvulsant therapy for plasma levels of 25-hydroxycholecalciferol (25-HCC), as measured by a specific competitive protein-binding assay. Mean values were 15.8±1.4ng/ml in adults and 16.3±1.6 in adolescents, in contrast with 4.8±0.8 in epileptic patients (difference from normal adults $t=5.55$, $p<0.001$). Two further epileptic patients with anticonvulsant osteomalacia responded quickly to administration of 25-HCC by mouth in doses of 10-45 μg daily, whereas Case 1 did not respond to calciferol in a dose of 45 μg daily by mouth, and Case 2 had well-marked osteomalacia despite a daily vitamin D supplement of 500 units for a period of over 1 year. The abnormally low 25-HCC levels found among the epileptic patients probably reflect alterations in vitamin D metabolism, since diet and sunshine exposure were considered adequate in them. (17 refs.) - *B. J. Grylack.*

Metabolic Ward
University College Hospital
London W.C.1, England

2446 **MILLICHAP, J. GORDON.** Drug treatment of convulsive disorders. *New England Journal of Medicine*, 286(9):464-469, 1972.

General principles of anticonvulsant therapy include the recommendations that: factors known to lower the seizure threshold be corrected when possible; a careful description of the pattern of the seizure be obtained as well as an EEG record; the optimum anticonvulsants be avoided; side effects be closely supervised; regular anticonvulsant therapy be introduced in the treatment of major epilepsy; and withdrawal of medications be carried out gradually and under supervision. Major seizure patterns (grand-mal, status epilepticus, and infantile spasms) are delineated. Minor seizure patterns include petit mal, myoclonic seizures, and akinetic seizures. Psychomotor seizure patterns are manifested by mental, motor, and sensory symptoms. The Jacksonian seizure and autonomic seizures and borderline epilepsy are described under focal seizure patterns. A number of drugs are listed for the treatment of these various patterns. (12 refs.) - *A. C. Schenker.*

720 N. Michigan Ave.
Chicago, Illinois 60611

2447 **PARKER, CHARLES E.; HARRIS, NANCY; & MAVALWALA, JAMSHED.** Dyke-Davidoff-Masson syndrome. *Clinical Pediatrics*, 11(5):288-292, 1972.

Pathogenetic and dermatoglyphic studies of 5 MR children exhibiting the Dyke-Davidoff-Masson syndrome indicate that this syndrome is a clinically recognizable entity, but that its causal factors probably vary considerably. The syndrome is characterized by MR, seizures, and cerebral hemiatrophy with homolateral hypertrophy of the skull

and sinuses. Additionally, all 5 children exhibit varying degrees of visual and perceptual problems, as well as language or speech disorders. Dermatoglyphic patterns were within normal ranges, indicating a probable late onset of the characteristic asymmetry. (7 refs.) - *N. Mize.*

Children's Hospital of Los Angeles
Los Angeles, California 90027

2448 **BOROFSKY, L.; LOUIS, S.; & ROGINSKY, M.** The pharmacology and efficacy of diphenylhydantoin in children. *Neurology*, 22(4):421, 1972. (Abstract)

The relationships between diphenylhydantoin (DPH) dosage, blood levels, and clinical efficacy were studied in 53 children and young adults from birth to age 20 years. In 80% of the children, the blood level (microgm/ml) was expressed as equal to 1-3 x dose (mg/kg). The remaining 20% represented 2 distinct populations: one whose blood level (microgm/ml) was equal to 3-4 x dose (mg/kg) and another whose blood level was equal to 0-1 x dose. Studies of DPH in seizure control involved the separation of the children into 4 groups: 10 children in whom the blood level reflected seizure control definitely, the seizures occurring at lower but not higher blood levels; 8 patients who were controlled with DPH (4-19 microgm/ml), but not with other medication; 20 children in whom DPH appeared to control seizures, although proof was lacking; and 12 children in whom control of seizures could not be achieved by the drug within the therapeutic dosage. - *A. C. Schenker.*

2449 **KNAUSS, THOMAS A.; & MARSHALL, RICHARD.** Neonatal seizures. *Neurology*, 22(4):419, 1972. (Abstract)

The influence of birthweight on the etiologies and prognosis of neonatal seizures was analyzed. Ss were 94 infants hospitalized in the Premature Center of the University of Washington; more than half of the seizures occurred during the first 24 hrs of life and 86% occurred within the first 72 hrs. Eighteen Ss weighed less than 1,500gm at birth; 27 weighed between 1,501 and 2,500gm; and 49 weighed more than 2,500gm. Etiologies for the Ss with lowest weights were perinatal and infectious; mortality rate was 61% and morbidity in survivors, 43%; 8 autopsied infants revealed subarachnoid, subependymal, intraventricular, and subdural hemorrhages. The medium weight Ss had similar etiologies and included respiratory failure and developmental anomalies; mortality rate was 44% and morbidity in survivors was 46%. Autopsy findings in 8 infants were similar to those in the low weight group. Principal etiologic correlates in the highest weight Ss were perinatal factors and developmental anomalies. Mortality rate was 35%; morbidity rate in survivors, 40%. In 12 autopsied infants there were 5 subarachnoid and 3 subdural hemorrhages. Overall the mortality associated with neonatal seizures is highly correlated with hemorrhage in the central nervous system. - *A. C. Schenker.*

2450 **SPEIDEL, B. D.; & MEADOW, S. R.** Maternal epilepsy and abnormalities of the fetus and newborn. *Lancet*, 2(7786):1088, 1972. (Letter)

In a study of maternal epilepsy and abnormalities of the fetus and newborn, the experimental and control groups were matched roughly for past obstetric history, social class, and sex of baby. The incidence of miscarriage in the pregnancies of all the epileptic women was 10% as compared with 8.9% in the controls. Ss in both groups were selected from 3 different maternity units with fairly clear social class distinctions, and there was a male to female sex ratio of 1 to 1.1 for both groups, with no preponderance of males among the malformed children. - *B. J. Grylack.*

Southmead Hospital
Bristol BS10 5NB, England

2451 **MACNAUGHTON, M. C.** Maternal epilepsy and abnormalities of the fetus and newborn. *Lancet*, 2(7786):1088, 1972. (Letter)

Before the findings of Dr. Speidel and Dr. Meadow with regard to a correlation between maternal epilepsy and fetal and newborn abnormalities can be accepted, it is important to know whether the 2 study groups were matched for past obstetric history, social class, and sex of baby. It is known that women with previous miscarriages or a previous fetal abnormality are more likely to have fetal abnormality in a subsequent pregnancy, that a strong association exists between neural-tube and

possibly other defects and social class, and that most congenital abnormalities occur more often in males, except for neural-tube defects. - *B. J. Grylack.*

Royal Maternity Hospital
Glasgow G4 ONA, Scotland

2452 **FEDRICK, JEAN.** ABO blood-groups and epilepsy. *Lancet*, 2(7785):1034, 1972. (Letter)

A previously unreported correlation has become apparent between ABO blood groups and epilepsy in pregnant women. ABO and rhesus blood groups were recorded for 164 of 168 women suffering from epilepsy who delivered between January 1966 and December 1970 in Oxfordshire and Berkshire (England). While the proportion of Rh-negative women among the epileptic series was similar to that among a control group of women delivered in the same area during 1968, the ABO blood group distribution differed significantly due to an excess of 18 epileptic women with A and AB blood groups. The A blood group was predominant both among women who had epilepsy since childhood and among women with later onset. (4 refs.) - *B. J. Grylack.*

Department of the Regius Professor
of Medicine
Oxford, England

2453 Status epilepticus. *British Medical Journal*, 1(5798):460-461, 1972. (Editorial)

The mortality rate of status epilepticus (2 or more major convulsions without return to consciousness or convulsions lasting 1 hr or more) has been decreased from 30-50% to 3 to 21%. In 54 epileptic patients with status epilepticus (excluding acute head injury) 19 had tumors, 13 had vascular lesions, 9 had infections, 13 had old injuries, congenital abnormalities, or metabolic disorders, and no cause was found in 32 of 86 patients. Cessation of anticonvulsant therapy frequently precipitated status epilepticus in epilepsy; brain tumor (single focal lesion in the frontal lobe) was frequently found. The treatment is to stop the cerebral dysrrhthmia with parenteral administration of anticonvulsants and to manage the cardiorespiratory symptoms. (10 refs) - *V. J. Goldberg.*

2454 **VIUKARI, N.M.A.; KAUKO, K.; & TAMMISTO, P.** Anticonvulsant hypocalcaemia. *British Medical Journal*, 2(5816):768-769, 1972. (Letter)

Phenytoin and phenobarbitone may form insoluble complexes with Ca salts which interfere with intestinal absorption of Ca^{+2} and drugs. Substituting a lactose excipient for $CaSO_4$ in phenytoin capsules resulted in increased blood levels of the drug. Twelve of 21 MR epileptics receiving phenytoin had mean Ca^{+2} of 4.37 ± 0.28 vs. 5.02 ± 0.23 in untreated controls (p less than 0.001), and all patients had normal Ca^{+2} levels in the CSF. The drug may interfere with the protein binding of Ca^{+2} and consequently with ion transport. (8 refs.) - *V. J. Goldberg.*

Research Department
Rinnekoti Institute for the
Mentally Retarded
Majalampi, Finland

2455 **SNYDER, C. HARRISON.** Conditions that simulate epilepsy in children. *Clinical Pediatrics*, 11(8):487-491, August 1972.

A thorough history-taking is probably the best means of preventing the all-too-common erroneous diagnosis of epilepsy in children. Twenty diseases or syndromes of extracerebral origin which may mimic epileptic seizures are reviewed as an aid to the physician who is faced with the task of diagnosing convulsions or other conditions of unexplained origin in children. (7 refs.) - *N. Mize.*

Alton Ochsner Medical Foundation
New Orleans, La. 70121

2456 **CUMMINGS, NANCY P.; *ROSENBLOOM, ARLAN L.; KOHLER, WILLIAM C.; & WILDER, B. J.** Plasma glucose and insulin responses to oral glucose with diphenylhydantoin therapy. *Pediatrics*, 51(6): 1091-1093, 1973.

The effect of diphenylhydantoin (DPH) (in the usual therapeutic doses for chronic seizure control) on glucose homeostasis was studied in children who were bing treated with DPH for seizure

disorders; this study was pursued because of reports of hyperglycemia and hypoinsulism in connection with toxic doses of DPH. The Ss were 20 children and adolescents who had been taking DPH from 100-400mg daily for at least 6 mos. Glucose was administered to the fasting Ss as a cola flavored drink at 1.75gm/kg body weight; blood samples were taken before and at 30min, 1, 2, 3 and 4hr after glucose ingestion. The only significant differences between patient and control groups were in the fasting and 4-hour insulin levels, which were higher in the DPH-treated group; no individual patient had an abnormal glucose tolerance test. There was no correlation between DPH serum levels and glucose values or peak insulin response. All reported instances of hyperglycemia related to DPH therapy have been in persons showing signs of neurologic toxicity. It would be of interest to determine if there is consistent abnormality of glucose and insulin in patients with neurotoxicity from DPH. (19 refs.) - *A. C. Schenker.*

University of Florida
Gainesville, Florida 32601

2457 Are anticonvulsants teratogenetic? *Lancet*, 2(7782):863-864, 1972.

A current report cites twice as many major congenital anomalies among babies born to epileptic mothers in Leeds, England, receiving anticonvulsant drugs as compared with a control group. The most common anomalies were congenital heart defects, cleft lip and palate, and nervous system malformations. The incidence of major abnormalities was lower than in a small, comparable Dutch survey. It was higher than in a large German survey in which half the mothers were not receiving anticonvulsants. Six of the Leeds babies had severe spontaneous hemorrhages. Despite the occurrence of major anomalies and serious bleeding disorders, the case against anticonvulsants can only be suggestive, not proven. (8 refs.) - *B. J. Grylack.*

MEDICAL ASPECTS—Chromosomal

2458 MANN, JOHN; & RAFFERTY, JOANE H. Cri-du-chat syndrome combined with partial C-group trisomy. *Journal of Medical Genetics*, 9(3):289-292, 1972.

A female infant with clinical features of the cri-du-chat syndrome and other physical abnormalities received the abnormal B group chromosome of her mother and the normal one of the maternal C group pair with a resulting monosomic state for a small portion of the B short arm and a trisomic state for a portion of the C long arm. Measurement data combining length and centromere index findings and thymidine and fluorescent data suggested that the translocation (T_1) chromosome was the one which had to be defined as No. 5 and that the T_2 chromosome was no 11. (5 refs.) - *B. J. Grylack.*

Kaiser Foundation Hospital
Santa Clara, California

2459 TURNER, GILLIAN; ENC'ISCH, BERT; LINDSAY, DAVID G.; & TURNER, BRIAN. X-linked mental retardation without physical abnormality (Renpenning's syndrome) in sibs in an institution. *Journal of Medical Genetics*, 9(3):324-330, 1972.

Study of the physical features and family histories of 18 inst MR male sib pairs showed that 11 pairs had no physical abnormality and that the majority in this group had a family history compatible with an X-linked entity. There were 2 affected female relatives as compared with 17 affected male relatives on the maternal side of the family. The finding of 11 pairs of sibs with presumptive Renpenning's syndrome in a small population in contrast to a single pair with phenylketonuria suggested that Renpenning's syndrome represents the most common cause of moderate MR in males (excluding Down's syndrome) and that it may well contribute significantly to the overall excess of males among the moderately MR population. (11 refs.) - *B. J. Grylack.*

Royal Alexandra Hospital for Children
Sydney, Australia

2460 SURANA, RAWATMAL B.; HUNT, TREVOR M.; & CONEN, PATRICK E. Multiple congenital defects associated with

an abnormal unclassifiable karyotype. *Journal of Medical Genetics*, 9(2):247-249, 1972.

A male infant born with orbital hypertelorism, a capillary hemangioma near the right eyebrow, coloboma of the left iris and choroid, corneal opacities, low-set ears, enlarged heart, marked cardiomegaly and pulmonary vascular congestion, bilateral gross hydronephrosis and hydroureter, and dermatoglyphic anomalies had a karyotype that could not be classified. Autoradiographic studies were inconclusive, and the banding pattern of the chromosomes was inadequate. A G/G translocation-Down's syndrome and isochromosome for the long arm of No. 21, trisomy 22 with a G/G translocation, and trisomy 16 with monosomy G were ruled out by various clinical and laboratory findings. Trisomy 17 with 17/G translocation or monosomy G with isochromosome for the short arm of one of the group C or B chromosomes remain possibilities. - *B. J. Grylack.*

Howard University College
of Medicine
Washington, D. C. 20001

2461 ATKINS, LEONARD; MILLER, WALTER L.; & SALEM, MARIA. A ring-20 chromosome. *Journal of Medical Genetics*, 9(3):377-380, 1972.

A ring-20 chromosome was seen in a 7-year-old MR boy with a behavior problem, seizures, and microcephaly. The abnormal chromosome probably originated in a parental gonad or in an early division of the zygote following breakage on both sides of the centromere, with subsequent ring formation and deletion of some chromosomal material. It is possible that the chromosomal breakage in the No. 20 of the propositus was due to administration of therapeutic dosages of anticonvulsant drugs. If this is the case, however, random chromosome breakage and rearrangements would probably have occurred rather than the observed consistent abnormality involving a single chromosome. (4 refs) - *B. J. Grylack.*

Massachusetts General Hospital
Boston, Massachusetts

2462 SCHOEPFLIN, GERALD S.; & CENTERWALL, WILLARD R. 48,XYYY: a new syndrome? *Journal of Medical Genetics*, 9(3):356-360, 1972.

A case of 48,XYYY, the second to be reported, was diagnosed by means of fluorescent and heterochromatin staining techniques in a 9-year-old boy. The propositus, his parents, and his sibs are in the seventy-fifth centile for height. His retarded-bone age suggests that he may reach greater height than that of his normal sibs. The most likely mechanism accounting for the extra Y chromosomes in this case is probably nondisjunction in spermatogonial mitosis followed by a second nondisjunction of one of the Y chromosomes in meiosis, which resulted in the formation of a sperm bearing 3 Y chromosomes. Long-term followup on growth, development, and personality patterns is continuing. (14 refs.) - *B. J. Grylack.*

Department of Pediatrics
Loma Linda University School
of Medicine
California 92354

2463 CASPERSSON, TORBJORN; LINDSTEN, JAN; ZECH, LORE; BUCKTON, KARIN E.; & PRICE, WILLIAM H. Four patients with trisomy 8 identified by the fluorescent and Giemsa banding techniques. *Journal of Medical Genetics*, 9(1):1-7, 1972.

Four patients showed an extra, apparently homologous chromosome, identified as No. 8 in all cases by the fluorescence and Giemsa banding techniques. Mosaicism could be demonstrated in 2 cases. The clinical pictures of the 4 propositi varied greatly. In contrast to the female proposita, the 3 males suffered from MR, not amounting to severe subnormality, concomitant strabismus, clinodactyly, and other skeletal defects. The female had a normal mental and physical development. Comparison of the findings with cases in the literature indicated that chromosome No. 8 might have been involved in some previously published reports. The fact that the mean maternal age was 32.2 years and the mean parental age 33.2 years for these 4 patients plus 1 published previously suggested possible etiologic significance for increased parental age in the origin of trisomy 8. However, it was impossible to elucidate the origin of the mosaicism. Chromosome No. 8 is the largest autosome found thus far among liveborn trisomics in man. (19 refs.) - *B. J. Grylack.*

Institute for Medical Cell Research
and Genetics
Stockholm, Sweden

2464 MITTWOCH, URSULA. Mongolism and sex: a common problem of cell proliferation? *Journal of Medical Genetics*, 9(1):92-95, 1972.

Potentially important findings on mitotic cycle time in plants, on cultured cells from patients with mongolism, and on human sex chromosomes indicate that mitotic cycle times and rates of cell proliferation may be dependent upon the particular chromosomal constitution involved. A lengthening of the mitotic cycle time can cause a slowing down of the cell proliferation rate and, thus, retardation of growth. Studies of the effect of different chromosomal constitutions on the differential rates of cell multiplication suggest that the addition of a particular chromosome to the normal karyotype could have not only a general effect on the length of the mitotic cycle but might also exert a more specific influence on the differential mitotic rate at this stage. The difference in mitotic cycle time between normal karyotypes with XX and XY chromosomes is generally slight, the rate of cell proliferation probably being somewhat higher in mammalian males than females. Gonadal rudiments of chromosomal males have been shown to grow significantly faster than those of their female litter mates in some animals. The mongol karyotype has not had a chance to be modified during evolution, and the addition of an extra chromosome 21 results in an abnormal developmental rate. (45 refs.) - *B. J. Grylack.*

University College
London NW1 2HE, England

2465 MULLER, H.; BUHLER, E. M.; SIGNER, E.; EGLI, F.; & STALDER, G. R. Trisomy-18 syndrome caused by translocation or isochromosome formation. A case report with bibliography. *Journal of Medical Genetics*, 9(4):462-467, 1972.

A female child presenting with the clinical and pathological characteristics of Edwards' syndrome had 21 normal pairs of autosomes and 2 X-gonosomes but only 1 chromosome No. 18. The second and additional third chromosomes 18 were replaced by 2 metacentric chromosomes, the large one consisting mainly of 18 long-arm material and the small one primarily of 18 short-arm material. Either a translocation trisomy resulted from nondisjunction after break events in both chromosomes 18 under consideration, or the isochromosome formation of both products of a transverse centromeric break occurred in a chromosome 18 in meiosis I. A bibliography of other cases in the literature is provided. (67 refs.) - *B. J. Grylack.*

University Children's Hospital
Basel, Switzerland

2466 DE CHIERI, PRIMAROSA R.; ALBORES, JOSE M.; COSIN, ABRAHAM; & COSIN, J. MARCELO. A human ring C chromosome associated with multiple congenital abnormalities. *Journal of Medical Genetics*, 9(2):239-242, 1972.

A 3-month-old female infant with bilateral epicanthal folds, small head circumference, bird-like facies, big ears, long and thin fingers, adduction of the fifth toe, a prominent heel, and angiomata plana in the frontonasal region and over her back had a ring C chromosome in peripheral blood lymphocytes and bone marrow cells. The location of the ring chromosome suggested that the chromosome change was widespread in the body and probably derived from one of the parental gametes. Autoradiographic examination of lymphocytes suggested a late-labeling, normal appearing X chromosome but did not further identify the ring chromosome, which appeared to be one of the longer autosomes of the C group. (5 refs.) - *B. J. Grylack.*

Instituto Nacional de Microbiologia
Carlos G. Malbran 111a
Buenos Aires, Argentina

2467 HAUKSDOTTIR, HALLA; HALLDORSSON, SAEVAR; JENSSON, OLAFUR; MIKKELSEN, MARGARETA; & MCDERMOTT, ALAN. Pericentric inversion of chromosome No. 13 in a large family leading to duplication deficiency causing congenital malformations in three individuals. *Journal of Medical Genetics*, 9(4):413-421, 1972.

Abnormal karyotypes were found for the 2 survivors among 3 children with congenital malformations, all members of a large family. Various peculiar craniofacial features, genital abnormalities, polydactyly, and other abnormalities of the extremities, accelerated growth in early life, and MR were predominant. Chromosomal analysis of 14 phenotypically normal family members revealed an abnormal karyotype differing from that of the 2 abnormal children. A pericentric inversion of chromosome 13 was confirmed by mitotic studies using labeling and fluorescent staining and by meiotic studies on 1 carrier. The abnormalities observed in the 3 children, 2 of whom were ascertained cytologically, were considered to be due to a crossover in meiosis between the inverted chromosome and its homologue in the carrier parent. Since these 3 children resembled each other much more than their own sibs and parents, it was felt that they might constitute a new syndrome associated with a specific chromosomal abnormality. (10 refs.) - *B. J. Grylack.*

Genetics Committee of the University
of Iceland
Reykjavik, Iceland

2468 **FAED, MICHAEL; MORTON, HUGH G.; & ROBERTSON, JANET.** Ring F chromosome mosaicism (46,XY,20r/46,XY) in an epileptic child without apparent haematological disease. *Journal of Medical Genetics*, 9(4):470-473, 1972.

A male child with epilepsy since age 4 and no evident hematologic disease or blood group abnormality was shown by the fluorescent banding technique to have a ring chromosome replacing chromosome 20 in 43% and 60% of cells in stimulated cultures harvested at 48 and 72 hours, respectively. Constitutional ring chromosomes have not been reported, apparently, for the F group, and even duplications or deletions involving a chromosome in this group have been rare. In the present case, material was probably lost from the long arms of the chromosome. There was no sign of polycythemia vera. (14 refs.) - *B. J. Grylack.*

University of Dundee
Dundee, United Kingdom

2469 **REISS, JACOB A.; WYANDT, HERMAN E.; MAGENIS, R. ELLEN; LOVRIEN, EVERETT W.; & HECHT, FREDERICK.** Mosaicism with translocation: autoradiographic and fluorescent studies of an inherited reciprocal translocation t(2q+;14q-). *Journal of Medical Genetics*, 9(3):280-286, 1972.

A male infant with multiple malformations and psychomotor retardation showed 2 cell lines in cultured lymphocytes, one containing a translocation involving a chromosome No. 2 and a D chromosome interpreted as 46,XY,t(2q+;Dq-), and the second being identical except for an additional Dq- chromosome. The severe growth and developmental retardation and malformations in the propositus presumably were related to the presence of the cell line with the extra chromosome, a cell line that was trisomic for the short arm, centromere, and a large portion of the proximal part of the long arm of chromosome 14 and a small portion of the distal part of the long arm of chromosome 2. The balanced 46,XY,t(2q+;14q-) cell line seen in the propositus, his father, and paternal grandfather represented the result of alternate segregation. (12 refs.) - *B. J. Grylack.*

University of Oregon Medical School
Portland, Oregon 97201

2470 **TUNCBILEK, ERGUL; ATASU, METIN; & SAY, BURHAN.** Dermatoglyphics in trisomy 8. *Lancet*, 2(7781):8821, 1972. (Letter)

A 3-year-old MR boy with multiple physical abnormalities and an extra No. 8 chromosome in the C group in approximately 25% of his cells showed dermatoglyphic findings which closely resembled those previously reported in the Penrose case. Prominent characteristics included both whorls and an arch on the fingertips, low total ridge count, tendency to high pattern intensity on both palms, irregular 4-finger line on the right palm, distally displaced axial triradii, and high pattern intensity on the soles. The close similarities between the 2 cases suggested that the peculiar dermatoglyphic patterns are characteristic for this chromosomal aberration. - *B. J. Grylack.*

Hacettepe University School of Medicine
Ankara, Turkey

2471 **DODSON, W. E.; AL-AISH, M. S.; &**

ALEXANDER, D. F. Cytogenetic survey of XYY males in two juvenile court populations, with a case report. *Journal of Medical Genetics*, 9(3):287-288, 1972.

Cytogenetic screening of a random sample of 475 males from juvenile court populations revealed only a single chromosomal abnormality. A boy had a supernumerary small metacentric chromosome in all 60 cells analyzed in 2 separate cultures, an abnormality not present in either parent. No patients with Klinefelter's syndrome, XYY, or structural rearrangements were detected. One of 6 patients seen on referral was found to have a 47,XYY karyotype. This S, a 17-year-old male, was more active and generally larger than his peers from birth and had a history of problem behavior. (7 refs.) - *B. J. Grylack.*

National Institute of Child Health
and Human Development
Bethesda, Maryland

2472 **HAUSMANN, LOTHAR; & GOEBEL, KLAUS-M.** Turner's syndrome with menstruation. *Journal of Medical Genetics*, 9(1):100-102, 1972.

A rare combination of Turner's syndrome with regular menstruation since age 14 and a 45,X karyotype was seen in a 20-year-old girl with epicanthus, gothic palate, micrognathia, a suggestion of cutis laxa, funnel chest, hyperelasticity of the joints, bilateral cubitus valgus, and hypoplastic skeletal muscles. While an earlier report concluded that a single X chromosome is capable of guaranteeing a full generative fertility, other findings have been interpreted to mean that the XX cells have to be present for the ovaries to function regularly. (8 refs.) - *B. J. Grylack.*

University of Marburg
d-3550 Marburg, Germany

2473 **ARMENDARES, SALVADOR; BUENTELLO, LEONOR; SALAMANCA, FABIO; & CANTU-GARZA, JOSE-MARIA.** A dicentric Y chromosome without evidence of sex chromosomal mosaicism, 46,XYqdic, in a patient with features of Turner's syndrome. *Journal of Medical Genetics*, 9(1):96-100, 1972.

A 16-year-old girl presented with features of Turner's syndrome, bilateral streak gonads in the position ordinarily occupied by ovaries, and a dicentric Y chromosome, but no evidence of mosaicism could be found. Both parents had normal karyotypes. The abnormal chromosome of the proposita, approximately twice the length of the father's Y chromosome, with 2 clearly visible centromeres, had characteristic autoradiographic, morphologic, and fluorescent patterns. The lack of support for mosaicism suggested that 46,XYqdic was the most likely karyotype. The observed stability of the dicentric Y chromosome was thought to be due to the fact that the 2 centromeres were situated sufficiently close to act as one, or perhaps because 1 of the centromeres was dominant. The possibility that factors on the long arm as well as on the short arm of the human Y chromosome play a part in male determination could not be excluded, since histologic study showed epididymal structures and suggested that some testicular differentiation during embryogenesis induced normal development of Wolffian ducts. (19 refs.) - *B. J. Grylack.*

Department of Medical Genetics
Hospital de Pediatria
Centro Medico Nacional
Av. Cuauhtemoc 330
Mexico 7, DF, Mexico

2474 **FAED, M.J.W.; WHYTE, R.; PATERSON, C. R.; MCCATHIE, MARGARET; & ROBERTSON, JANET.** Deletion of the long arms of chromosome 18 (46,XX,18q-) associated with absence of IgA and hypothyroidism in an adult. *Journal of Medical Genetics*, 9(1):102-105, 1972.

A mildly MR 21-year-old girl with hypothyroidism and a deletion of long arm material from chromosome 18 presented with the small stature, poor muscular tone, carp mouth, midfacial hypoplasia, and internal strabismus characteristic of cases of the Eq- syndrome, but her fingers were short and showed a complete absence of whorl patterns. Her gross reduction in serum immunoglobulin A, in association with deletions from either end of the chromosome, may be linked to the observation that only 1 allele for immunoglobulin production

appears to be active in any one cell. (20 refs.) - *B. J. Grylack.*

University of Dundee
Dundee, United Kingdom

2475 **GRIPENBERG, ULLA; ELFVING, J.; & GRIPENBERG, L.** A 45,XX,21- child: attempt at a cytological and clinical interpretation of the karyotype. *Journal of Medical Genetics*, 9(1):110-115, 1972.

A case of a 45,XX,21- karyotype together with minor somatic anomalies and signs of MR in a female child seemed consistent with true 21-monosomy, but a hidden translocation was not ruled out entirely. Chromosomal material had evidently been lost, since the number of centromeres was only 45, and a piece the size of a G group chromosome was missing. A reciprocal translocation between No. 21 and an unknown chromosome could have been followed by the loss of the smaller translocation chromosome containing material of both of the chromosomes involved. However, such loss of chromosomal material usually results in more generalized and major malformations than were seen in the present case. No addition of chromosomal material to any member of the complement could be detected cytologically. (21 refs.) - *B. J. Grylack.*

University of Helsinki
Helsinki, Finland

2476 **NEVIN, N. C.; DODGE, J. A.; & ALLEN, INGRID V.** Two cases of trisomy D associated with adrenal tumours. *Journal of Medical Genetics*, 9(1):119-122, 1972.

Two unrelated male infants had trisomy D associated with adrenal tumors. Multiple abnormalities were present at birth in both propositi. Case 1 had a large adrenal cortical carcinoma, rarely seen in D-trisomy, and died at age 15 days. Case 2 had a microscopic neuroblastoma in the adrenal medulla and died at age 4 days. This tumor is frequently seen as an incidental finding in infants who die under 3 months of age and has been associated with various cytogenetic findings. (14 refs.) - *B. J. Grylack.*

The Queen's University of Belfast
Belfast, Northern Ireland

2477 **WINTER, J.S.D.; AHLUWALIA, K.; & RAY, M.** Congenital hypothyroidism in association with a ring chromosome 18. *Journal of Medical Genetics*, 9(1):122-126, 1972.

A girl aged 10 years 9 months presented with a ring chromosome 18 and congenital hypothyroidism. This represented the third case in which hypothyroidism was reported in association with partial monosomy 18. The failure to find any cells from the proposita with a normal karyotype suggested that the ring chromosome originated before fertilization. Her MR, microcephaly, and short stature were probably a result of untreated hypothyroidism, at least in part, but the rounded facies, low hair line, high arched palate, and club feet noted at birth appeared to be related more directly to the chromosomal abnormality. The hypothyroidism seemed to be a result of synthesis of an abnormal iodinated peptide. (6 refs.) - *B. J. Grylack.*

Winnipeg Children's Hospital Research Foundation
Manitoba, Winnipeg, Canada

2478 **VIANNA, ANGELA M.; FROTA-PESSOA, OSWALDO; LION, MARCOS F.; & DECOURT, LUIS.** Searching for XYY males through electrocardiograms. *Journal of Medical Genetics*, 9(2):165-167, 1972.

Electrocardiographic screening was attempted with a large sample of clinically normal males in order to ascertain double-Y males. Of approximately 30,000 electrocardiograms collected over a 7-year period, 34 were selected because they were normal except for having P-R intervals of 0.2sec or more and belonged to a population of normal males under 50 years of age who were not taking drugs. Of 11 Ss whose karyotypes were studied, a tall, middle class man with an apparently normal son and daughter had a P-R interval of 0.24sec and a 47,XYY chromosome complement. Each of the other 10 Ss showed a 46,XY karyotype, but 2 of them, with P-R intervals of 0.22 and 0.20sec, respectively, had an abnormally long Y chromosome. Of 3 other males with enlarged P-R intervals subsequently added to this sample, 2 had a 46,XY karyotype with an abnormally long Y chromosome. The finding of 1 XYY individual among 14 presenting prolonged P-R intervals was

very suggestive of a high association between these 2 abnormalities. (3 refs.) - *B. J. Grylack.*

Universidade de Sao Paulo
Sao Paulo, Brazil

2479 **COOKE, PATRICIA; BLACK, J. A.; & CURTIS, DIANA J.** Comparative clinical studies and X chromosome behavior in a case of XXXX/XXXXX mosaicism. *Journal of Medical Genetics*, 9(2):235-238, 1972.

A female child representing the second case of XXXX/XXXXX mosaicism was shown by chromosomal, autoradiographic, and buccal smear analysis to have an approximately 50:50 mosaicism between a 48 chromosome cell line with 3 supernumerary X chromosomes and a 49 chromosome cell line with 4 supernumerary X chromosomes. The supernumerary X chromosomes in both cell lines behaved independently of each other with regard to interphase condensation and late-labeling behavior. Comparison of the clinical descriptions of the 9 other cases of XXXX or XXXX/XXXXX with the present case indicated the difficulty of defining any specific clinical features or characteristic facies but suggested that mental subnormality and dwarfism, together with some abnormalities of the feet and hands, are usual, while a congenital cardiac abnormality may be present in approximately a third of cases. (13 refs.) - *B. J. Grylack.*

The University
Highfield, Southampton SO9 5NH,
England

2480 **BLACKSTON, R. DWAIN; & CHEN, ANDREW T. L.** A case of 48,XXXX female with normal intelligence. *Journal of Medical Genetics*, 9(2):230-232, 1972.

A 48,XXXX female child first examined at 3 years 9 months and given follow-up testing at age 5 showed normal intellectual potential despite slow speech development. The proposita probably represented an exception to the previously reported definitive correlation between 48,XXXX females and MR, although her normal IQ could be explained on the basis of an undetected chromosomal mosaicism. Clinical findings were not entirely consistent with features observed in other tetra X females. Some dermatoglyphic features were also unusual. (9 refs) - *B. J. Grylack.*

Emory University School of Medicine
Atlanta, Georgia

2481 **SCHMIDT, RINA; MUNDEL, GEORGE; ROSENBLATT, MALKA; & KATZ-NELSON, MARIASSA BAT-MIRIAM.** Apparent G-monosomy, G-deletion, and incomplete Down's syndrome in a single family. *Journal of Medical Genetics*, 9(4):457-461, 1972.

A family was reported in which 2 female children displayed some features of Down's syndrome but apparently had normal karyotypes, a male sib was retarded and had an apparent complete monosomy G, and the phenotypically normal mother had a deletion of the long arms of 1 of her G chromosomes. The 2 sisters died at 4 months of age. During meiosis, the deleted maternal G-group chromosome was lost, but the translocated segment, probably on the C-group chromosome, was apparently preserved, thus accounting for the survival of the male child. The translocated G-group chromosomal mass inherited from the mother probably accounted for the mongoloid features of the 2 girls. The chromosomal analyses of the mother and the 2 girls and the clinical picture of these children with many features of Down's syndrome provided support for the theory that complete autosomal monosomy is incompatible with life. (18 refs.) - *B. J. Grylack.*

Asaf Harofe Government Hospital
Zrifin, Israel

2482 **SMITH, G. F.; JUSTICE, PARVIN; & HSIA, D.Y.Y.** Blood enzymes in the de Lange syndrome. *Journal of Medical Genetics*, 9(2):172-173, 1972.

Enzyme studies of 10 to 20ml of heparinized blood obtained from de Lange patients and matched controls showed minor differences between the two groups, but none was statistically significant. The values for the de Lange patients were generally more variable, suggesting greater heterogeneity, but there was no evidence of any consistent blood cell enzyme changes. (8 refs.) - *B. J. Grylack.*

Stritch School of Medicine
Loyola University
Maywood, Illinois

2483 **SINGER, J.; SACHDEVA, SHANTA; SMITH, G. F.; & HSIA, D.Y.Y.** Triple X female and a Down's syndrome offspring. *Journal of Medical Genetics*, 9(2):238-239, 1972.

A 30-year-old triple X female with normal intelligence gave birth to a child with Down's syndrome at age 29 and is functioning as an adequate housewife and mother. Nothing about her physical appearance indicated that this woman possessed an extra X chromosome. This seems to be the first example of a triple X female giving birth to a child with a chromosomal abnormality. (5 refs.) - *B. J. Grylack.*

Stritch School of Medicine
Loyola University
Maywood, Illinois 60153

2484 **COHEN, MAIMON M.; & DAVIDSON, RONALD G.** Double aneuploidy (47,XX,21+/45,X) arising through simultaneous double non-disjunction. *Journal of Medical Genetics*, 9(2):242-244, 1972.

A newborn female represented a unique case of double aneuploidy which probably arose as a result of two simultaneous postzygotic nondisjunctional events within a single cell leading to 2 leukocyte stem lines, 47,XX,21+ and 45,X. The few leukocytes with 46 chromosomes all possessed the extra No. 21 and provided evidence of random loss from other chromosomal groups, but cultured skin fibroblasts yielded only the 47,XX,21+ karyotype. The findings were probably a result of chimerism or mosaicism, these nondisjunctional events being involved in an interpretation of the data on the basis of mosaicism. (36 refs.) - *B. J. Grylack.*

State University of New York
School of Medicine
Buffalo, New York 14222

2485 **MORIC-PETROVIC, SLAVKA; LACA, ZIVANA; & KALICANIN, PREDRAG.** Down's syndrome with an atypical G/G translocation derived from familial pericentric inversion in one chromosome of the G group. *Journal of Medical Genetics*, 9(4):478-482, 1972.

A male child with Down's syndrome was the son of a woman who had one chromosome in the G group with an unusual appearance, as her two sisters did. This marker chromosome, assumed to represent a pericentric inversion (46,XX,G inv,p+q-), differed from the other G group chromosomes in having the long arm shortened, while the short arm was elongated in the same way as in the propositus. The phenotype of the propositus probably resulted from an error during meiosis in the mother subsequent to the pericentric inversion of her G chromosome. (4 refs.) - *B. J. Grylack.*

Human Cytogenetic Laboratory
Belgrade, Yugoslavia

2486 **KAJII, TADASHI; OHAMA, KOSO; AVIRACHAN, SUGANDHI; & AVIRACHAN, THOMAS T.** Trypsin banding of Giemsa-stained chromosomes. *Lancet*, 2(7790):1311-1312, 1972. (Letter)

Use of conventional Giemsa-stained slides for trypsin banding has yielded good banding patterns in slides up to 7 days old. The method allows for parallel studies of chromosomes before and after banding and is also convenient in cases where material is not available for reexamination or there is a limited number of slides to be analyzed. (3 refs.) - *B. J. Grylack.*

Laboratory of Embryology and
Cytogenetics
University Clinic of Gynaecology
and Obstetrics
Geneva, Switzerland

2487 **BOBROW, M.; COLLACOTT, H.E.A.C.; & MADAN, K.** Chromosome banding with acridine orange. *Lancet*, 2(7790):1311, 1972. (Letter)

A technique that is relatively reliable has been developed for reverse banding of chromosomes utilizing 0.01% acridine orange. This dye stains quinacrine-negative regions a bright green-yellow, while the quinacrine or Giemsa-band regions are a dull red-orange. Approximately 70% of slides examined by this technique were found to yield adequate banding. On the basis of examination of a possible nonreciprocal translocation (13q+,18q-) by this technique, it was concluded that the

exchange of telomeres assumed to occur had indeed taken place. (3 refs.) - *B. J. Grylack.*

M.R.C. Population Genetics Unit
Old Road, Headington
Oxford OX3 7LE, England

2488 CROSSEN, PETER E. Human-chromosome banding. *Lancet*, 2(7783):920-921, 1972. (Letter)

Study of the factors affecting the banding patterns of human chromosomes has shown the interval between slide-making and treatment to be of great significance. The clearest banding patterns have come from slides a week old, treated for 2 minutes in NaOH followed by 2 hours in phosphate buffer and stained for 5 minutes in 10% Giemsa. Good banding has also been achieved by allowing an interval of 6 to 8 days before treatment with trypsin. The variability of most banding methods is attributable to the state of "hardness" of the DNA/protein complex of the chromosome. (6 refs.) - *B. J. Grylack.*

Cytogenetics Unit
Christchurch Hospital
Christchurch, New Zealand

2489 JACKSON, JOHN F.; CLEMENT, ELVIE G.; NORTH, EDWARD R., III; & WOOSLEY, PAUL. Chromosome breakage as a dosimeter. *Lancet*, 2(7783):920, 1972. (Letter)

Peripheral blood leukocytes were scored for chromosome breakage for 202 patients, 5 of whom had been exposed to LSD or irradiation. The other 197 patients were 113 Ss with clinical abnormalities but a normal modal chromosome number, 67 with clinical abnormalities and aneuploid chromosome modes, and 17 with no clinical abnormalities and normal modal chromosome numbers. In the 5 Ss with suspected increased chromosome breakage, 11 of 149 cells contained breaks, yielding a rate of 0.0738 breaks per cell, which is not quite statistically different from that for the combined control population (0.0398). In the clinical application of chromosomal analysis using peripheral blood lymphocytes as a dosimeter in man, the problem of obtaining a significant difference is greatly increased. The establishment of normal population aberration rates and the achievement of adequate sample sizes for evaluation of individual analyses both present difficulties. (2 refs.) - *B. J. Grylack.*

University of Mississippi Medical
Center
Jackson, Mississippi 39216

2490 CIRNU-GEORGIAN, LILIANA; & CIOLTEI, ANCA. Identification of deleted chromosome segments. *Lancet*, 2(7782):878-879, 1972. (Letter)

Examination of chromosomes in blood cultures from a woman with primary amenorrhea revealed a deleted X chromosome in 80% of observed metaphases. Immersion of the slides in a trypsin solution and treatment with Giemsa stain showed the deleted segment to be on the short arm of an X chromosome, near the centromere. Analysis of banding patterns should make it possible to locate homologous segments of the X and Y chromosomes and to match structural abnormalities of the X chromosome with their phenotypic effects. (10 refs.) - *B. J. Grylack.*

Dr. Victor Babes Institute of
Pathology and Medical Genetics
Bucharest, Rumania

2491 LOTT, IRA T.; MURPHY, DENNIS L.; & CHASE, THOMAS N. Down's syndrome. Central monoamine turnover in patients with diminished platelet serotonin. *Neurology*, 22(9):967-972, 1972.

Nine Down's syndrome patients were compared with 12 non-MR controls with respect to platelet 5-hydroxytryptamine (5-HT) levels and the concentration of 2 monoamine catabolites in cerebrospinal fluid before and during probenecid administration. Platelet 5-HT levels averaged about 60% less in Down's syndrome patients than in controls. Statistical differences were not found between the 2 groups with regard to steady-state concentrations of 5-hydroxyindoleacetic acid (5-HIAA), the principal catabolite of 5-HT, and homovanillic acid (HVA), a major catabolite of dopamine, in cerebrospinal fluid and the effect of probenecid on 5-HIAA and HVA in the fluid. The results failed to corroborate the hypothesis that low levels of platelet 5-HT in Down's syndrome reflect a defect in the central transport or metabolism of the

indoleamine. (37 refs.) - *B. J. Grylack.*

Laboratory of Clinical Science
National Institute of Mental Health
Bethesda, Maryland 20014

2492 **DAHL, G.; & ANDERSEN, H.** Chromosome studies in 30 children with Turner's syndrome. *Acta Paediatrica Scandinavica*, 61(1):17-23, 1972.

Thirty children with Turner's syndrome were investigated for chromosomal patterns, sex chromatin, and blood group determinations. Fifteen patients had a 45,X karyotype without mosaicism, 2 patients had 46,XXqi, 1 had a normal female karyotype, and 12 had mosaicism in which 1 cell line was always 45,X and the other was either normal male or normal female karyotype or showed an abnormality of 1 X chromosome. Four patients with mosaicism 45,X/46,XXr or 45,X/46,XXq- were sex chromatin negative like the 45,X, while both patients with 46,XXqi were sex chromatin positive. In all, 21 patients were sex chromatin negative, 4 were sex chromatin positive, and 5 had sex chromatin in a lower number than in normal females. The data indicated that sex chromatin determination is not adequate as a screening test for X chromosome abnormality in Turner's syndrome. In patients with sex chromatin positive distribution, normal female karyotype or an isochromosome for the long arm of an X chromosome is expected, whereas mosaicism of the karyotype is usual in patients with sex chromatin in a lower number than in normal females. Xg blood group determination in 23 patients and their parents revealed a paternal origin of the missing X or abnormal X chromosome in 4 patients. In 2 additional cases the abnormal X chromosome was probably of paternal origin. (9 refs.) - *B. J. Grylack.*

Vaerebrovej 77
2880 Bagsvaerd, Denmark

2493 **NIELSEN, JOHANNES.** Immunological aberrations in patients with aneuploid chromosome abnormalities and in their parents. *Humangenetik*, 16(2):171-176, 1972.

Studies of immunological reactions in patients with aneuploid chromosome aberrations were reviewed to investigate the possibility of a correlation between autoantibody formation and aneuploidy. Among Turner's syndrome and Down's syndrome patients, there are several reports of significant thyroid autoantibody reactions. Mothers of Down's patients have increased thyroid antibody titer, but a similar correlation for the mothers or fathers of Turner's and Klinefelter's patients was not found. These findings suggest that the tendency to form thyroid antibody and the tendency to nondisjunction might be related. (16 refs.) - *V. J. Goldberg.*

Statshospitalet Risskov
DK-8240 Risskov, Danmark

2494 **SUBRT, I.; & BERANKOVA, J.** Clinical case reports: a case of 18p- syndrome. *Humangenetik*, 16(4):359-360, 1972.

An 11-month-old girl with growth and psychomotor retardation was diagnosed to have 18p-syndrome. Clinical findings included facial dysmorphia (internal epicanthus, mongoloid slant, hypertelorism, and retrognathia), short neck, prominent ears, general hypotony, hypoplastic digits, and right simian crease. DQ was 55. IgA was absent. Karyotype revealed a deletion in the short arm of chromosome 18. The patient conforms to other cases of 18p with relatively mild anomalies, in contrast to 5 reported cases with holoprosencephaly incompatible with life. - *V. J. Goldberg.*

Charles University
Prague, Czechoslovakia

2495 **GOUW, W. L.; ANDERS, G.J.P.A.; TEN KATE, L.P.; & DEGROOT, C. J.** Paternal transmission of a B/D translocation, t(4p–; 14p+ or 15p+), resulting in a partial 4p trisomy. *Humangenetik*, 16(3):251-259, 1972.

A 2½-yr-old boy had MR, marked asymmetry of the skull and thorax, mild scoliosis, hypertelorism, high arched palate, hypospadias, bilateral simian creases, trunk ataxia, and intention tremors in the extremities. The father's sibship included cases of MR and convulsive disorders. Dermography of the father revealed low a-b ridge count. Karyotypes revealed normal maternal pattern and very large Y chromosomes in the patient and father. Autoradiographic studies revealed that the father was a balanced carrier of B/D reciprocal translocation of

the type t(4p–; 14p+ or 15p+). The patient was probably trisomic for part of the short arm of chromosome 4 and monosomic for part of the short arm of 14 or 15. Heavier than expected labeling of number 4 chromosome was observed in the patient's cells, but no satellites on the 4p chromosome were found, indicating that the chromosomal combination is the result of an adjacent -1 segregation at paternal meiosis. The phenotype has no specific characteristics and probably depends on the length of the translocated or missing segment as well as the consequences of the possible position effects. (10 refs.) - *V. J. Goldberg.*

Anthropogenetisch Institut
Groningen, The Netherlands

2496 PASSARGE, EBERHARD. Spontaneous chromosomal instability. *Humangenetik*, 16(2):151-157, 1972.

Cultured cells which are homozygous for Fanconi's anemia (fa), Bloom syndrome (b1), ataxia telangiectasia (att), and xeroderma pigmentosum (xd) have spontaneous chromosomal instability. Affected individuals have increased risk of malignancy. There may be genetic and clinical heterogeneity in xd and fa. The incidence of metaphase changes (including chromatid and isochromatid breakage, acentrics, dicentrics, reunions, minutes, pulverizations, and polyploids) ranges from 15 to 25% in fa and bl. The distribution of anomalies is a function of culture length, with tetraploids, acentrics, and pulverizations increasing, and chromatid and isochromatid breaks decreasing. The differences in distribution in chromosome anomalies between 1b and fa include random involvement of homologous chromosomes in reunion figures in fa (in one case 55 of 240 had homologous interactions) and nonrandom involvement in B1 (in 1 case 37 of 42 reunion figures were between homologous chromosomes). (11 refs.) - *V. J. Goldberg.*

Institut fur Humangenetik
Hamburg, W. Germany

2497 SCHULER, D.; FEKETE, G.; & DOBOS, M. Mit einen alkylierenden Agens (Zitostop) *in vitro* induzierbare Mutationen bei Malignomen und bei Syndromen, die zur Malignitat disponieren. (Mutations induced *in vitro* by an alklating agent [Zitostop] in malignant disease and in syndromes predisposing to malignancy). *Humangenetik*, 16(4):329-336, 1972.

The number of chromosome mutations induced in cultured lymphocytes by the alkylating agent Zitostop depends on the individual. The number of induced mutations was higher than controls in cells from Down's syndrome patients (which is accompanied by a higher incidence of malignancy) and in 2 members of a "cancer family." An increase in mutations in some of the cases was observed in ataxia telangiectasia and in complete remission phase of acute lymphoid leukemia. It is debatable whether the use of an alkylating agent to induce chromosome mutations is a suitable procedure for detection of increased mutability. (6 refs.) - *V. J. Goldberg.*

Kinderklinik der Medizinischen
Universitat
"Semmelweiss"
Budapest, Hungary

2498 GEISLER, M.; KLEINEBRECHT, J.; & DEGENHARDT, K. -H. Histologische Analysen von triploiden Spontanaborten (Histological analysis of spontaneous abortions with triploidy). *Humangenetik*, 16(3):283-294, 1972.

Three of 4 triploid abortions (gestational age 14 to 21 wk) displayed true triploidies (2 69, XXY; 1 69, XXX) and 1 mosaic (46, XX/ 69, XXY, 1:1). The placentae all displayed hydatiform generation, and normal development had stopped at gestational age of 21 to 31 days. Two embryos were recovered and found to have malformations in the central nervous system and caudal region. Arrest of external feature development occurred at 28 to 30 days, and organogenesis ceased at ovulational age of 5 to 5½ wk. (42 refs.) - *V. J. Goldberg.*

Institut fur Humangenetik
Frankfurt, W. Germany

2499 NIEBUHR, E. Localization of the deleted segment in the cri-du-chat syndrome. *Humangenetik*, 16(4):357-58, 1972.

Fluorescence studies of 17 cri-du-chat syndrome patients revealed that the chromosome abnormality is the deletion from the short arm length (from 15 to 80%) of chromosome #5. The deletion of the 5p15 and part of 5p14 bands

appears to be sufficient for expression of the syndrome. More extensive deletions are not associated with increased clinical findings. (3 refs.) - *V. J. Goldberg.*

John E. Kennedy Institute
DK-2600 Glostrup, Denmark

2500 **ROSENKRANZ, W.; & HOLZER, S.** Satellite association. A possible cause of chromosome aberration. *Humangenetik*, 16:127-150, 1972

Satellite association (SA) of acrocentric chromosomes was determined in metaphase of blood cultures. In 45 cultures of 15 normal males there were 32.6 ± 14.7 SA in 100 metaphases and in 45 cultures of 15 normal females there were 39.2 ± 12.0 SA ($P > 0.01$), Down's syndrome boys had 49.5 SA ($P < 0.01$ compared to normal males) and Down's syndrome girls had 58.9 SA ($P < 0.01$ compared to normal women). Down's syndrome children had 54.2 SA vs 27.2 for normal children ($P < 0.001$); distinct increases were also found in cultures of parents of mongoloid children, although data were not significant enough to justify SA association as a reliable predictor of recurrence. Klinefelter's XXY males had 43.8 SA ($P<0.001$ compared to normal men). There were no correlations of Turner's syndrome, trisomy E, and parents of Down's patients and SA. Association tendency in females implies heterochromic X influence on SA. (9 refs.) - *V. J. Goldberg.*

Institut fur Medizinische
Biologie und Humangenetik
A-8010 Graz, Austria

2501 **KIRMAN, BRIAN H.** Genetic counselling. *British Medical Journal*, 2(5804):46, 1972. (Letter)

The threefold increased risk reported for a subsequent sib being affected by Down's syndrome throughout the maternal age range is similar to the overall increased risk to a mother who has had 1 affected child irrespective of her age or the type of chromosome anomaly. However, it has been shown that most of the increased risk is due to balanced translocation or factors other than maternal age. (2 refs.) - *B. J. Grylack.*

Queen Mary's Hospital
for Children
Carshalton, England

2502 **WALLER, H.; & WALLER, M.** Chromosomenmosaik 46,XY,D-, t(DqGq) + /92, XYXY,2D-,2t(DqGq)+ bei einem Saugling mit Down-Syndrom (Chromosome mosaic 4 6 , X Y , D - , t (D q G q) + /92,XYXY,2D-,2t(DqGq)+ in an infant with Down's syndrome. *Humangenetik*, 17:99-104, 1973.

Because of the rare occurrence of polyploids in man and the problem of interpreting *in vitro* preparations of such chromosome anomalies, the case of a 7-week-old infant with diploid-tetraploidy-mosaic with an additional tertiary trisomy (translocation trisomy) is reported. In this case, the tetraploid cells constituted a phenomenon which could only be attributed to explantates of the lung as the source and not to any spontaneous alteration *in vitro*. (19 refs.) - *A. C. Schenker.*

Pathologisches Institut
der Martin Luther-Universitat
Halle-Wittenberg, Germany

2503 **MICHAELSON, P. S.; & GILLES, F. H.** Central nervous system abnormalities in trisomy E (17-18) syndrome. *Journal of the Neurological Sciences*, 15(2):193-208, 1972.

The neuropathologic findings in 11 cytogenetically proven cases of trisomy E(17-18) syndrome are reviewed. Abnormalities of telencephalic external topography, hippocampus, lateral geniculate body, and brainstem were present in all cases. Abnormality of the lamellae of the inferior olivary nuclei was present in 10 cases. Nonspecific microscopic findings in the brains of these patients were cerebellar dysplasias, cerebellar heterotopias, cerebral heterotopias, white matter astrocytosis, and subarachnoid glial islands. Dysplasias of the paraflocculus ventralis or of the lingula of the cerebellum were present in 10 cases. The terminal result of perinatal telencephalic leukoencephalopathy could be the paucity of the white matter of the cerebrum as seen in 2 cases. Abnormality of

the dentate nucleus of the cerebellum was noted in 6 cases. (37 refs.) - *A. C. Schenker.*

Harvard Medical School
Boston, Massachusetts

2504 **ESBER, HENRY J.; BARBARICH, MICHAEL; MENNINGER, FLORIAN F., JR.; MESHORER, EDWARD; MONEDJIKOVA, VIRGINIA; & ROSENKRANTZ, HARRIS.** Hepatitis-associated antigen and immunoglobulin composition in patients with Down's anomaly. *American Journal of Clinical Pathology*, 59(6):872-876, 1973.

The relationship between immunoglobulin composition, Australia antigen, and Down's syndrome was investigated by simultaneous determination of serum proteins, IgA, IgG, IgM, and hepatitis-associated antigen (HAA) in patients with Down's syndrome and in normal volunteers. The results revealed that 65% of the 26 patients with Down's syndrome had HAA; all had marked increments in IgG of about 80% ($p<0.01$); there was a 27% drop in IgA in patients with HAA ($p<0.05$). Patients with Down's syndrome had lower concentrations of α_1-globulin, α_2-globulin, and β-globulin, and an increase in γ-globulin. The elevation of IgG levels in the patients suggests a chronic response to infectious agents rather than immunological malfunctions. (17 refs.) - *A. C. Schenker.*

Mason Research Institute
Wrentham, Massachusetts

2505 **COOKE, PATRICIA.** Age-related variation in the number of secondary associations between acrocentric chromosomes in normal females and patients with Turner's syndrome. *Humangenetik*, 17:29-35, 1972.

Data are presented on age-related variation in 123 normal females and 36 patients with Turner's syndrome. Chromosome preparations were made by the separated leukocyte method; the number of associations and number of D and G group chromosomes in a 30-cell sample were scored for each individual. In the normal female set, the pattern of change with respect to age revealed a rise in association frequency to age 16-20, followed by a gradual fall at age 41-45, results fluctuating thereafter. No significant differences in association frequency with age were found in patients with Turner's syndrome. The observed differences in association frequency between normal females of different ages and between normal females and patients with Turner's syndrome may be due either to differences in genotype or to differences in the serum environment of the cells. Evidence that serum constituents may affect association frequency comes from the study of the same individuals at different times. It appears from the present work that the number of nucleolar associations declines with age; this reduction may be associated with a reduction in the number of organized nucleoli or with a lower frequency of fusion events between the nucleoli. (7 refs.) - *A. C. Schenker.*

The University of Southampton
Hants SO9 5NH, Great Britain

2506 **BARLOW, PETER.** The influence of inactive chromosomes on human development: anomalous sex chromosome complements and the phenotype. *Humangenetik*, 17:105-136, 1973.

The effect of heterochromatin on cell division and some quantifiable phenotypic traits of individuals with sex chromosome anomalies which may be due to upsets in the coordination of mitotic cycles and differentiation are described. It was found that in human cells growing in culture, the presence of heterochromatic sex chromosomes slows cell division. If there are a number of cell types differentiating within an organ at different times along the developmental time scale, then the relative frequency of these cells could be markedly altered by a rate of cell division faster or slower than normal. Thus the presence of heterochromatin could bring about changes through its effect on cell division. Some phenotypic characteristics in individuals with sex chromosome anomalies can be quantified, using heterochromatin. Additional sex chromosomes are shown to depress quantitatively measurable traits such as dermatoglyphics, intelligence, birthweight, height, and immunoglobulin levels. The additional sex chromosomes are heterochromatic; the property of heterochromatin to reduce the rate of cell division may account for the effect produced by

extra sex chromosomes. (260 refs.) - *A. C. Schenker.*

A.R.C. Unit of Developmental
Botany
Cambridge, CB3 ODY, England

2507 RAAIJMAKERS-ENGELEN, ELLY W. I. Identification of D/D translocation in mentally retarded patients. *Humangentik*, 17:165-168, 1973.

The identification of 2 D/D translocations is reported, using a modified method which combines quinacrine fluorescence staining and enzymatic digestion. Routine chromosome analyses without banding techniques were performed on 2 patients with severe MR; all metaphases examined revealed 45 chromosomes with an additional A group chromosome, while 2 D group chromosomes were missing. The banding technique used showed that the 2 translocations (since both patients were regarded as carriers of a D/D translocation) had originated from different chromosomes; they were identified as a t(13q14q) and a t(14q15q). The technique also revealed which acrocentric chromosomes were involved and that the translocations consisted of the entire long arm of the D chromosomes. These translocations may have originated by centric fusion, which is considered as a Robertsonian type of chromosome rearrangement. (8 refs.) - *A. C. Schenker.*

Psychiatric Hospital
St.Anna, Venray, The Netherlands

2508 GOEMINNE, LUE. Synopsis of mammorenal syndromes. II. *Humangenetik*, 17:271-272, 1973.

Associated breast and renal abnormalities are described in rare dysmorphic syndromes of multiple primary congenital defects. Ear anomalies are also frequently found in these syndromes. The syndromes included: 18-trisomy, 18-long arm deletion, Cornelia de Lange, Smith-Lemli-Opitz, Fraser, and the olfacto-genital syndrome (Kallmann). (3 refs.) - *A. C. Schenker.*

Medical Clinic
B-9780 Zulte
Belgium

2509 MEHES, KAROLY. Paternal trisomy 21 mosaicism and Down's anomaly. *Humangenetik*, 17:297-300, 1973.

The apparently unaffected father of a child with Down's syndrome was found to be mosaic for trisomy 21, thus drawing attention to the possibility of paternal mosaicism. The first 17 cells examined in the blood culture of the father of a 1-year-old child with Down's anomaly proved to be 46,XY normal, but the eighteenth cell contained 47 chromosomes with an extra small acrocentric one. Upon a repeated examination of 40 cells, 3 were found with a trisomy G. In genetic counseling, maternal or paternal mosaicism justifies monitoring the pregnancies by examination of the amniotic cells. (8 refs.) - *A. C. Schenker.*

University Medical School
Pecs, Jozsef Attila u. II, Hungary

2510 GARDNER, R.J.M.; VEALE, A. M. O.; & SANDS, VALERIE E. XXXX syndrome: case report, and a note on genetic counseling and fertility. *Humangenetik*, 17:323-330, 1973.

The clinical findings in 10 XXXX females are summarized and the report of a new case with this syndrome is presented. The girl, aged 14 years and 10 months, first presented with language difficulties and later with epilepsy. Other features of this case were: a peculiar facial appearance, skeletal abnormalities, EEG abnormalities, and intellectual and psychological retardation. The patient had contracted renal inflammation prior to seizure episodes; this may have acted as sufficient stimulus for a lowered convulsive threshold. A review of the known cases suggests that a common mechanism, faulty chromosome distribution at maternal meiosis I and II, brought about a majority of XXXXY, XXXXX, and XXXY cases. The shortwave diathermy given to the mother at the time of conception may have caused nondisjunctions of the oocyte. In the absence of any other aneuploid family member, genetic counseling can probably be encouraging in these cases. Fertility in XXXX females may be reduced. (26 refs.) - *A. C. Schenker.*

Auckland Medical School
Auckland, New Zealand

2511 EGLI, F.; & STALDER, G. Malformation of kidney and urinary tract in common chromosomal aberrations: I. Clinical studies. *Humangenetik*, 18:1-15, 1973.

Renal and urinary tract anomalies associated with chromosomal aberrations are reviewed, as well as such malformations in a normal population. Any single malformation of the urinary system occurs in a normal population at the most with a frequency of a few per thousand, except for hydronephrosis, which occurs at about 2-4 per hundred. In postmortem findings in 55 cases of trisomy D-syndrome, the incidence of renal anomalies is over 60%. In 95 cases of trisomy E, the incidence was 69.5%; in 141 cases with trisomy 21, 4 patients had renal agenesis or hypoplasia and 1 patient had horseshoe kidney. In a review of postmortem findings of 103 children with Down's syndrome, only 6.7% showed renal abnormalities. In all 6 cases of cat-eye syndrome, renal anomalies were present. In chromosome-4 short-arm deletion, chromosome-18 long-arm deletion, and 18-ring chromosome, renal malformations have been detected in a lower but significant percentage. In patients with cri-du-chat syndrome (5p-), chromosome-13 long-arm deletion, 13 ring chromosome and 18 short-arm deletion, and in Klinefelter's syndrome, malformations of the kidney occur only occasionally. No renal anomaly can be correlated to a specific chromosome or chromosomal area. (285 refs.) - *A. C. Schenker.*

Universitats-Kinderklinik
CH-4000 Basel
Switzerland

2512 MILUNSKY, AUBREY. Sex-determining genes and the Y-chromosome. *New England Journal of Medicine*, 288(11):587, 1973.

The developmental sequence of sex determination, with or without the Y-chromosome, which is usually linked with male phenotype expression, is discussed. On rare occasions, in the apparent absence of Y-chromosomes, and with a 46 XX karyotype, a male phenotype is observed; moreover, a female phenotype may be observed with a 46 XY karyotype. The general appearance and psychosexual orientation of the XX individuals are male; many of their features are similar to those found in Klinefelter's syndrome. Gynecomastia, deficient Leydig-cell function and testicular tubule hyalinization, and fibrosed and lacking spermatogonia are often found in these individuals. Diagnosis by karyotype is recommended to prevent confusion with Klinefelter's syndrome. True hermaphrodites, possessing XX karyotype, can be distinguished from XX males by gonadal biopsy. The developmental sequence appears to be that the bipotential embryonic gonad, influenced by an autosomal gene for maleness, develops into a testis. When the Y-chromosome is present, it acts in a regulatory manner, allowing normal testicular development. (4 refs.) - *A. C. Schenker.*

2513 TONDURY, G. Malformations of kidney and urinary tract in common chromosomal aberrations: II. Morphogenetic studies. *Humangenetik*, 18:16-32, 1973.

Morphologic changes of the renal abnormalities in common chromosomal aberrations are summarized and correlated with known events of embryonic development. The majority of malformations in man arise as a result of damage suffered by the embryo between the twentieth and the fortieth day. Among the abnormalities in the D and E trisomy syndromes, renal malformations are very common. The pattern of abnormalities, which varies in different autosomal trisomies, includes: Horseshoe kidney, megalureter, abnormalities of position, unilateral and/or double kidney, double ureters, hydronephroses, and polycystic renal cortex. In human embryos, the mesonephros begins to differentiate on day 28, the ureteric bud on days 28-30, and, during the seventh week (33± 1 days), the kidney starts to slide forward over the ridges formed by the umbilical arteries. Renal malformations are connected with impaired development of the ureteric bud. Double ureters associated with renal abnormalities were detected in early human embryos of 8 to 10mm in length. Congenital pelvic kidney is the result of a failure of ascent of the kidney; fusion of the lower poles may result in a horseshoe kidney; and congenital polycystic kidneys are the result of urine secretion in tubuli lacking a normal outlet. (10 refs.) - *A. C. Schenker.*

Anatomisches Institut der Universitat
Ch-8006 Zurich
Switzerland

2514 KOVACS, M.; SELLYEI, M.; SZABO, A.; & VASS, L. Occurrence of XYY individuals among juvenile delinquents in Hungary. *Humangenetik*, 18:85-87, 1973.

The association of XYY chromosome complement with extreme body height and antisocial behavior prompted a study of quinacrine-stained buccal smears from an unselected group of 173 adolescent male delinquents in Hungary. Body height varied between 154 and 191cm; the criminal offenses committed were theft, rape, and vagrancy. In one case, 30% of cells had 2 Y chromatins and all 50 mitoses, analyzed from lymphocyte culture, possessed an XYY-sex chromosome complement. This person was 180cm in height and had been sentenced repeatedly for theft and vagrancy. Although quinacrine stained buccal smears provide a reliable method of identifying double Y cases, interpretation of the results must be cautious, especially when this structure is less than 30%. (5 refs.) - *A. C. Schenker.*

Semmelweiss Medical University
Budapest IX, Hungary

2515 **ALBERMAN, E.; POLANI, P. E.; ROBERTS, J. A. FRASER; SPICER, C. C.; ELLIOTT, M.; & ARMSTRONG, E.** Parental exposure to X-irradiation and Down's syndrome. *Annals of Human Genetics*, 36(2):195-208, 1972.

Preconception radiation histories of 465 parents of children with Down's syndrome were compared with corresponing histories of 465 parents of children with other congenital defects which are not thought to be associated with parental irradiation. It was concluded that maternal radiation does play some part in the etiology of Down's syndrome, particularly in mothers of the older age-groups, but that paternal radiation does not. The findings suggest that the maximum effect is produced by radiation occurring more than 10 years before conception. It is possible that radiation damage by small doses, added to aging, may be a factor in the genesis of primary trisomy 21. Results are compared with those of reports in the literature. (35 refs.) - *A. C. Schenker.*

Pediatric Research Unit
Guy's Hospital Medical School
London SE 1 9RT, England

2516 **ALBERMAN, E.; POLANI, P. E.; ROBERTS, J. A. FRASER; SPICER, C. C.; ELLIOTT, M.; ARMSTRONG, E.; & DHADIAL, R. K.** Parental X-irradiation and chromosome constitution in their spontaneously aborted foetuses. *Annals of Human Genetics*, 36(2):185-194, 1972.

Histories of medical radiation received by parents of spontaneous abortuses of abnormal karyotype were compared with corresponding histories in cases of abortions of normal karyotype and with those of parents of live births. The findings in the abortuses suggest that 845 mothers of chromosomally abnormal abortuses have received the largest mean gonadal dose of irradiation for medical reasons compared with the other spontaneous abortions and the live birth controls. The mean gonad dose of mothers of triploids exceeded that of the other groups of chromosomally abnormal abortuses with a positive maternal irradiation history. Triploidy is the second commonest specific chromosome anomaly in spontaneous abortions, and it would seem that irradiation might have an additive effect on the production of triploid fetuses. (17 refs.) - *A. C. Schenker.*

Pediatrics Research Unit
Guy's Hospital Medical School
London S. E. 1 9 RT, England

2517 **MATSUNAGA, EI; & TONOMURA, AKIRA.** Parental age and birth weight in translocation Down's syndrome. *Annals of Human Genetics*, 36(2):209-217, 1972.

The effects of parental age upon births of translocation trisomics and an examination of differences in birthweight between translocation trisomics and 21-trisomics are described. The data analyzed concerned 102 cases of translocation trisomics, 46 of which were collected by other investigators. These constituted 4.7% of the patients with Down's syndrome so far karyotyped. The results revealed that paternal age is irrelevant to the cases of either t(DqGq) or t(GqGq) trisomy, but maternal age did have an effect upon the production of those trisomics, the relative risk increasing for the t(GqGq) and decreasing for the t(DqGq) with age. The mean birthweight of Down's syndrome patients, irrespective of the karyotype or the sex, was much lower than the average population; the means of the 2 groups in the females were close to each other but the male 21-trisomic had a larger though not significant mean than the birthweight of the translocation trisomics. (18 refs.) - *A. C. Schenker.*

National Institute of Genetics
Mishima, Japan

2518 **SHIBATA, K.; WALDENMAIER, C.; & HIRSCH, W.** A child with a 21-ring chromosome, 45,XX,21-/46,XX,21r investigated with the banding technique. *Humangenetik*, 18:315-319, 1973.

Chromosomal analysis of lymphocytes and fibroblasts using staining techniques such as fluorescence and banding can be performed to verify and identify suspected chromosomal aberration. Such studies performed in a slightly MR infant with minor malformations showed a mosaicism 45,XX,G-/46,XXGr. Lymphocyte culture analysis showed 3 morphologically normal and one atypical chromosome present in group G in 91% of the cells. In 2 fibroblast culture analyses, 85% and 82%, respectively, of the cells investigated also showed a ring chromosome. The banding technique identified the anomalous chromosome as number 21, and verified a diagnosis of partial monosomy 21. Dermatoglyphs were also performed, which showed specific peculiarities of formation. Identification of chromosome pairs 21 and 22 by conventional methods is difficult; unambiguous identification can only be made by using one of the staining methods. Further similar cases should be investigated with staining techniques in order to clearly differentiate the characteristics and related clinical features of number 21 chromosomal aberrations. (15 refs.) - *C. Wares*.

Klinderklinik der FU Berlin
D-1000 Berlin 19, Germany

2519 **TANGHERONI, WILLY; CAO, ANTONIO; & FURBETTA, MARIO.** Multiple anomalies associated with an extra small metacentric chromosome: modified Giemsa stain results. *Humangenetik*, 18:291-295, 1973.

Giemsa chromosome stain techniques and characterization of associated multiple congenital anomalies may identify the small metacentric extra chromosome 18. In studies on an infant with multiple anomalies, clinical similarities associated with trisomy 18 syndrome were noted (failure to thrive, slow motor and mental development, abnormal facies, abnormal placement of ears, slight abnormality of extremities). Cytogenetic staining techniques (Giemsa) showed 47 chromosomes in the patient. The additional chromosome was an abnormal small metacentric chromosome without satellites. The size and banding pattern of the extra chromosome suggest that it could be an isochromosome, possibly for the short arm of chromosome 18. The association of the stain results with the clinical similarities of this case and cases of known trisomy 18 syndrome reinforce this suggestion. The comparison of chromosomal banding patterns found in such cases of multiple anomalies associated with an extra chromosome and of normal phenotypes with the same chromosome anomaly could be used to clarify the nature and origin of this chromosomal aberration. (24 refs.) - *C. Wares*.

University of Perugia
Italy

2520 **HECHT, FREDERICK; MAGENIS, R. ELLEN; & MCCAW, BARBARA K.** Clinical cytogenetics: dawn breaks on a new era. *American Journal of Diseases of Children*, 125(3):319-321, 1973.

The interaction of clinical cytogenetics with pediatrics is both highly productive and promising. From the simple techniques for analyzing metaphase chromosomes of which cytogenetics consisted prior to 1956, the specialized branch of cytogenetic medical knowledge has rapidly advanced. The human karyotype was characterized, important chromosomal abnormalities were discovered, and new mechanisms of inherited disease became known by 1965. In 1965 the field of cytogenetics began a period of consolidation and enrichment by means of statistical and case studies. New momentum for advancement in theory and research was gained in 1967-68 by the development of fluorescent microscopy with quinacrine mustard (QM) and in 1970 light microscopy with differential Giemsa (G) staining. These techniques eventually enabled researchers to stain and identify individual human chromosomes differentially. The QM technique is of special value in identifying the Y chromosome, while the G techniques also allow reliable chromosome identification at less expense. Reciprocal and insertional translocations in chromosome material may also be easily distinguished by either method and information used to predict and diagnose affected children. In 3 case studies, cytogenetic study of chromosomes specifically diagnosed the problems of Down's syndrome, Down's syndrome and carrier translocation type, XYY karotype, and reciprocal translocation. Such positive results of

pediatric interaction with cytogenetics suppose similar future synergy. (13 refs.) - *C. Wares.*

University of Oregon Medical School
Portland, Ore. 97201

2521 **CURTIS, DIANA J.** Chromosome number 18. *Humangenetik*, 18:273-277, 1973.

A modification of Seabright's (1971) method of banding human chromosomes may be used to identify chromosome abnormality. In 4 cases of "chromosome abnormality" unstained chromosome preparations were made from standard short-term leukocyte culture, and the material was differentially banded. Enzyme digestion was performed with suitable dilutions of a standard 5% trypsin solution with Sorensen's phosphate buffered saline. Diluted Leishman's stain was used to stain bands deep pink. Banded karyotypes were then prepared with reference to Leishman stained material. All 4 cases showed an aberrant complement of chromosome 18, with 3 diagnosed as E trisomy 18 and the fourth diagnosed as having a structural alteration of chromosome 18. Chromosome 18 in triplicate causes clinical features which are not normally lethal during fetal development, but may make independent neonatal survival unlikely. Deletion of part of chromosome 18 is apparently compatible with survival. New information on genetic information located on chromosome 18 may possibly be gained by comparison of genetic structural alterations and accompanying clinical features. (6 refs.) - *C. Wares.*

Centre for Human Genetics
Sheffield, 10, Great Britain

2522 **BOFINGER, MARY K.; DIGNAN, PETER ST. J.; SCHMIDT, ROSEMARY E.; & WARKANY, JOSEF.** Reduction malformations and chromosome anomalies. *American Journal of Diseases of Children*, 125(1):135-143, 1973.

Congenital reduction malformations are sometimes due to chromosomal anomalies, and the latter syndromes may be tentatively identified on the basis of associated malformations. Recognition of the importance of the cytogenetic basis of limb malformation may influence individual prognosis and genetic counseling, as prior theory and diagnosis have been concentrated upon environmental causation such as thalidomide. The association of multiple congenital malformations of the extremities and chromosomal anomalies has been documented in case studies of 3 such infants in whom cytogenetic studies were performed. Case 1 with reduction of the upper right extremity showed a karyotype of 46, XY, Br. Case 2 had congenital anomalies of the lower extremities and was found to have 47 chromosomes with an extra in the C group. Case 3 had anomalies of the upper extremities and also showed 47 chromosomes, with a karyotype of 47,XX,E+(18+). Numerous similar congenital reduction malformations had previously been reported in patients with chromosome anomalies in groups B, C, D, E, and G, sex chromosomes, and chromosome breakage. Patterns of these defect associations have been identified as diagnostic aids. (73 refs.) - *C. Wares.*

Children's Hospital Research
Foundation
Cincinnati, Ohio 45229

2523 **HIRSCHHORN, K.; LUCAS, MARY; & WALLACE, ISOBEL.** Precise identification of various chromosomal abnormalities. *Annals of Human Genetics*, 36(2):375-379, 1973.

Material from members of 8 different families was studied for precise identification of chromosomal anomaly; in 6 the abnormality was a chromosomal translocation, in one a pericentric inversion, and in one a trisomy. The method used was a modification of Seabright's method, based on treatment of the fixed chromosomes with trypsin; the modification included observations of pH and temperature, and preheating freshly prepared slides. The finding of 2 translocations involving chromosome number 10, with apparently identical break points (q11), suggests that certain portions of chromosomes may be more susceptible to breakage and rearrangement. The existence of trisomy 22 in a liveborn abnormal infant was proven, as well as a suspected pericentric inversion of chromosome 3 and the presence of a recombinant chromosome resulting from an intraloop crossover, which was accurately identified prenatally. (12 refs.) - *A. C. Schenker.*

Mount Sinai School of Medicine
New York, New York 10029

2524 **PYATKIN, E. K.; SUSKOV, I. I.; & PETROVA, S. A.** Influence of hypotonic treat-

ment on chromosome aberrations induced in human bone-marrow cells by gamma-rays. *Lancet*, 1(7741):100, 1972. (Letter)

A comparison study has demonstrated considerably more aberrant metaphases, chromatid-type aberrations, and paired chromosome fragments in human bone-marrow cells after hypotonic treatment with a potassium chloride solution than when a mixture of Hank's solution and distilled water was used. The types and frequencies of induced chromosome aberrations were compared after exposure of human bone-marrow cells to therapeutic gamma-rays. The observed differences in frequency associated with the two methods of hypotonic treatment are attributable to differential saturation of metaphases with aberrations – not to any differences in the actual number of aberrant metaphases. (3 refs.) - *N. Mize*.

Ministry of Public Health
Moscow D-182, U.S.S.R.

2525 **NEU, RICHARD L.; & GARDNER, LYTT I.** Banding patterns of the Y chromosome. *Lancet*, 1(7758):1020, 1972. (Letter)

The differences observed in banding patterns on the Y chromosome when the Giemsa staining method is used, as opposed to the quinacrine-mustard (Q.M.) fluorescent staining procedure, is most probably attributable to the light-emitting properties of Q.M. fluorescence. It seems likely that the same banding pattern actually exists, but that the fluorescence of Q.M. staining makes it impossible to distinguish between the two neighboring bands on the Y chromosome. The result is that the distal end of the long arm fluoresces brightly with Q.M. staining and with Giemsa staining shows two bands. (1 refs.) - *N. Mize*.

Upstate Medical Center
Syracuse, N.Y. 13210

2526 **DOYLE, P.; & BISHUN, N.** Simplified technique for demonstrating banding patterns in human chromosomes. *Lancet*, 1(7761): 1184, 1972. (Letter)

By only slightly modifying a known technique for demonstrating the banding patterns in human chromosomes, consistent and reproducible results can be obtained. The procedure is simple and results in uniformly stained chromosomes which greatly facilitate the study of banding patterns. The crucial determinant of this successful banding technique is heating, a process termed differential denaturation. (5 refs.) - *N. Mize*.

Marie Curie Memorial Foundation
Surrey, England

2527 **ANSEDE, ALICIA.** Human chromosome banding. *Lancet*, 1(7762):1184, 1972. (Letter)

A method for obtaining chromosome banding patterns from short-term cultures of whole blood has proven successful in 80% of the metaphases treated. Successful banding depends on an elapsed interval of 6-8 days from preparation of the cell spread to trypsin exposure. (1 ref.) - *N. Mize.*

University of Santiago de Compostela
Spain

2528 **DEV, V. G.; WARBURTON, D.; & MILLER, O. J.** Giemsa banding of chromosomes. *Lancet*, 1(7763):1285, 1972. (Letter)

In light of current research it seems probable that the Giemsa chromosome banding effect is produced by any pretreatment which removes divalent cations, rather than being related to the proteolytic activity of the enzyme preparations, as previously thought. Pretreatment of fixed metaphase chromosomes with a trypsin-containing solution known to bind calcium ions has produced excellent banding. In view of the narrow pH and temperature optima of trypsin, this effect is not likely attributable to enzyme reaction. Other reported pretreatment solutions, as well, are known to be deficient in Ca^{++} and Mg^{++}, providing further support for this hypothesis. (4 refs.) - *N. Mize*.

Columbia University College
of Physicians and Surgeons
New York, New York 10032

2529 **RIDLER, M.A.C.; & OHARA, P. T.** Ultrastructure of banded human metaphase chromosomes. *Lancet*, 1(7764): 1339-1340, 1972. (Letter)

Treatment with trypsin has been shown to facilitate the examination of banded human metaphase

chromosomes by electron microscopy. Previously, efforts to remove intact cells had proven extremely difficult. In the best preparations, at low magnification, the metaphase chromosomes of lymphocyte cultures were similar to those seen with the light microscope. These recent electron microscope observations support previous findings from other techniques that banding is mainly determined by chromosomal proteins and not by DNA. The release of protein from chromatin fibers by trypsin could explain the reduction in their size and reactivity. (5 refs.) - *N. Mize.*

Harperbury Hospital
Herts., England

2530 **HECHT, F.; & KIMBERLING, W. J.** Registry of data on Robertsonian (centric-fusion) translocations. *Lancet*, 1(7764):1342, 1972. (Letter)

A pilot computer chromosome registry, developed under contract with the National Institute of Child Health and Human Development, is beginning to log in data on known cases of Robertsonian centric-fusion translocations of the D/D, D/G, and G/G type. Robertsonian translocations, which occur in about 1 in 1,000 babies, were chosen because of their genetically interesting properties. The registry has been made feasible by the widespread availability of new cytogenetic techniques which allow for precise chromosome identification. So far data retrieval has proven to be relatively simple and inexpensive, a feature which enhances its potential value in genetic and epidemiologic research. (8 refs.) - *N. Mize.*

University of Oregon Medical School
Portland, Oregon 97201

2531 **SEVERN, DAVID J.** Heterozygote frequencies to calculate incidence of genetic disease. *New England Journal of Medicine*, 288(15):797, 1973. (Letter)

Conclusions drawn by Levy and Shih, regarding the detection of any rare genetic disorder, that such disorder cannot be determined without testing millions of infants by accurate methods in different populations, are held to be unduly pessimistic. When heterozygotes are detectable, calculations based on their frequency provide more reliable estimates of the incidence of homozygous recessives than can be obtained by direct counting. Homozygous recessives in relatively rare disorders do not provide an adequate sample size. It is doubtful whether testing millions of infants is as desirable as extracting maximum information from a single population by calculating the incidence indirectly from the heterozygote frequency. In testing children from different populations, the incidence of galactosemia, for example, may be significantly different, which might easily obscure the importance of the difference in genetic equilibria, if the two populations were added and used as one sample. - *A. C. Schenker.*

Sugar Association, Inc.
New York, New York

2532 **LELE, P. P.** No chromosomal damage from ultrasound. *New England Journal of Medicine*, 287(5):254, 1972. (Letter)

A series of 7 reports dealing with the effects of ultrasound on chromosomal morphology or cell reproduction appeared in the *British Journal of Radiology* while an editorial on the subject was in press (Lele, *N Engl J Med*, 286:1317-1318, 1972). In 6 reports, no damage could be attributed to ultrasound, and the authors of the seventh, dissenting report simply recommended caution in its clinical use. In general, the authors of the 7 reports are in agreement with the view expressed in the editorial concerning the diagnostic use of ultrasound. (2 refs.) - *V. J. Goldberg.*

Massachusetts Institute of Technology
Cambridge, Massachusetts

2533 **VAN DEN BERGHE, H.; VAN EYGEN, M.; FRYNS, J. P.; TANGHE, W.; & VERRESEN, H.** Partial trisomy 1, karyotype 46, XY, 12-,t(1q, 12p)+. *Humangenetik*, 18:225-230, 1973.

Multiple anomalies in a newborn male were found in association with a previously unreported trisomy of chromosome #1. The malformations of the infant included deviation of the sternum, absence of the gall bladder, and agenesis of the kidneys. The cardiac defects were a persistent truncus arteriosus originating entirely from the right ventricle (type II of Collett and Edwards) and a large atrial septal defect. These deformities may have been due to the arrest of cardiac development around day 40. Quinacrine fluores-

cence karyotypes of the child and his mildly MR mother revealed an abnormally large C-chromosome, and a partial deletion of the # 1 chromosome was found in the mother. The probable karyotype of the infant was 46, XY, 12-, t(1q, 12p)+. (20 refs.) - *V. J. Goldberg.*

University of Leuven
Leuven, Belgium

2534 BECH, KAREN; & TYGSTRUP, INGE. Down's syndrome and oestriol excretion in late pregnancy. *Lancet*, 2(7789):1261, 1972. (Letter)

The adrenals, livers, pituitaries, and placentae of 8 infants with Down's syndrome were examined to see whether anomalies of these organs can be associated with the low estriol excretion observed in late pregnancy among the mothers of Down's syndrome infants. Except for the histological finding of a hypoplastic fetal zone of the adrenal cortex in 3 to 8 S, there were no general anomalies in the organs which are supposed to be the sites of fetoplacental estrogen production. (3 refs.) - *V. J. Goldberg.*

Laboratory of Paediatric Pathology
University Hospital of Copenhagen
DK-2100 Copenhagen, Denmark

2535 MCDONALD, ALISON. Yearly and seasonal incidence of mongolism in Quebec. *Teratology*, 6(1):1-3, 1972.

The incidence of mongoloid births was studied in Quebec in the period between 1947 and 1967 to determine whether regular peaks in such births occur, as reported in the literature; 2,398 children with mongolism were registered between 1958 and 1967, a rate of 1.86/100 live births. For the 10-year period there was no evidence of any seasonal variation in monthly rates by year or in the total rates by month. Although there were epidemics of infectious hepatitis in the years 1961-63 in Quebec, no evidence of a correlation in the numbers of births of children with mongolism and such infections was found. Available evidence suggests that mongolism occurs at a fairly constant rate regardless of geographic location or race. (14 refs.) - *A. C. Schenker.*

2536 ROSENBLOOM, ARLAN L.; & FRIAS, JAIME L. Oxandrolone for growth promotion in Turner syndrome. *American Journal of Diseases of Children*, 125(3):385-387, 1973.

Oxandrolone treatment in the Turner syndrome is described in 9 patients, treated for periods of 4-34 months. The pretreatment growth velocity varied from 0.5cm/yr to 3.8cm/yr. Oxandrolone, administered in a dose of 0.075-0.125mg/kg of body weight once daily, increased the velocity of growth to an average of 5.3cm/yr. Five of the 6 patients treated for longer than 1 year showed a greater growth velocity during the first as compared to the second year of treatment. The only side effect noted was deepening of the voice in 3 of the girls. Treatment with oxandrolone in XO gonadal dysgenesis is recommended because of the 8-fold increase in linear growth velocity in a condition characterized by persistent slow growth and no adolescent growth spurt; the absence of undue acceleration of osseous maturation; and the taller average stature of treated girls with remaining growth potential than in adult patients not treated with androgens. Psychological effects of the delay in feminization have been modulated by adjunctive therapy with relatively low doses of estrogen. (19 refs.) - *A. C. Schenker.*

University of Florida
College of Medicine
Gainesville, Florida 32601

2537 STEIN, ZENA; SUSSER, MERVYN; & GUTERMAN, ANDREA V. Screening programme for prevention of Down's syndrome. *Lancet*, 1(7798):305-310, 1973.

Adaptation of the diagnostic procedure for Down's syndrome from a clinical measure for sporadic use into a screening device that will be used systematically with many pregnant women appears to be potentially useful and technically feasible. Although the estimated incidence of Down's syndrome at birth has been declining slightly, due to a reduction in the total numbers of children born and to demographic factors of maternal age, its prevalence is on the rise due to increased survival rate. The rise in the proportion of Down's syndrome among all cases of severe MR is also striking. A program of conception prevention might eliminate genetic transmission of the syndrome but would have little effect on the incidence in the population. Intervention after

conception through prenatal diagnostic screening is needed to reduce incidence. Such a program would involve amniocentesis, laboratory culture of aspirated cells for karyotype identification, induced abortion of affected fetuses, a comprehensive information service, and evaluation of the program in terms of effectiveness and ethics. An outline of a plan for mounting a screening program in New York City illustrates the operations and estimated effect of prenatal screening. (34 refs.) - *B. J. Grylack.*

2538 **GHOSH, M. L.** Congenital leukaemia and Down's syndrome. *Indian Journal of Pediatrics*, 39(298):379-382, 1972.

Congenital acute myeloblastic leukemia was seen in association with Down's syndrome in a female newborn. The infant looked healthy except for the typical features of Down's syndrome. There was no family history of malignancy, and the mother had neither been exposed to irradiation for the past 5 years nor suffered any infection during pregnancy. Clinical manifestations compatible with congenital leukemia began 3 days after birth and consisted of abnormal blood and bone marrow morphology with increased leukemic blast cells confirmed by cytochemical staining characters and a rapid fatal course. (24 refs.) - *B. J. Grylack.*

District General Hospital
Barnsley, Yorkshire, England

2539 **DUCHARME, J. R.; LETARTE, J.; LEBOEUF, G.; & COLLU, R.** Latent diabetes and gonadal dysgenesis. *Acta Paediatrica Scandinavica*, 62(1):99, 1973. (Abstract)

Ten patients with Turner syndrome were investigated for anomalies of carbohydrate metabolism and coexistence of autoimmune phenomena. Oral and intravenous glucose tolerance tests, intravenous tolbutamide, and conventional thyroid function tests were administered. Only 4 showed gonosomal mosaicism (2 XO/XX, 1 XO/XXr, and 1 XO/XX/XXX). Fasting blood sugar was less than 95mg% in 9 cases and 110mg% in 1 case. The rate of anomalies varied from 30% to 60%. Insulin release was abnormally low in more than 50% of the cases, and hypersensitivity to endogenous insulin was probable in 4 of the 9 patients tested with tolbutamide. The data suggested that the glucose disposal rate shows an inverse relationship to growth hormone release during oral glucose load. Thyroid antibodies by thyroglobulin hemagglutination and thyrotoxid gland complement-fixation were positive in 7 of 9 patients, and 4 showed definite evidence of thyroiditis. - *B. J. Grylack.*

2540 **FABRIS, C.; FRANCESCHINI, P.; BOGETTI, GABRIELLA; & PONZONE, A.** Sex chromosome anomalies detection and fluorescence. *Acta Paediatrica Scandinavica*, 62(3):307-308, 1973.

A 6-month-old boy referred for external genital abnormalities was found by chromosome analysis on peripheral blood cultures to have 2 cell lines, 45 chromosomes with 4 small acrocentrics (60%), and 46 chromosomes with 4 small acrocentrics and a ring chromosome (40%). Quinacrine fluorescence on metaphase plates gave ambiguous results, but examination of hair root and peripheral blood cells in interphase revealed a fluorescent corpuscle of such high frequency that it could not be attributed to intensely fluorescent regions of chromosomes other than Y. The presence of a Y chromosome in 1 of the 2 cell lines was confirmed by a subsequent diagnosis of mixed gonadal dysgenesis. This appears to be the first case of Y ring chromosome reported thus far. It may be the only condition in which interphase fluorescence can resolve questions raised by metaphase analysis. (2 refs.) - *B. J. Grylack.*

Paediatric Clinic
University of Turin
Turin, Italy

2541 **ANDERSSON, H.; FALLSTROM, S. P.; LUNDBORG, P.; & ROOS, B. -E.** 5-Hydroxyindoleacetic acid in children with Down's syndrome. *Acta Paediatrica Scandinavica*, 62(2):158-160, 1973.

A study of 5-hydroxyindoleacetic acid in the cerebrospinal fluid of 33 children (CA 2 days to 3.5 years) with Down's syndrome has indicated a progressive decrease with age from about "normal" to "subnormal" levels. During the first half year of life, levels of the mongoloid infants are in the same range as or even somewhat above those of the controls. From age 40 weeks on, however, levels of the mongoloid children are significantly lower than control values ($p<0.01$).

This progressive decrease could be due to a defective storage of 5-hydroxytryptamine neurons, with overfunctioning of the 5-hydroxytryptamine synthesizing neurons after some months resulting in an exhaustion (low 5-hydroxyindoleacetic acid levels at the end of the first year), or to the fact that the low rate of 5-hydroxyindoleacetic acid production, existing from birth, only becomes unmasked as low levels in cerebrospinal fluid at this time. (13 refs.) - *B. J. Grylack.*

University of Goteborg
Goteborg, Sweden

2542 MEISNER, LORRAINE F.; CHUPREVICH, THOMAS W.; & INHORN, STANLEY L. Nucleotide specificity of Giemsa banding. *Lancet,* 2(7820): 94-95, 1973. (Letter)

Clarification of the nature of protein components in Giemsa staining is presented due to misinterpretation of previous communications. The mechanism of Giemsa banding is not necessarily the same as quinacrine, but appears more complex, involving a DNA-protein azure-eosinate complex in some banding techniques. Also, since the secondary constrictions of human chromosomes 1 and 16 usually demonstrate Giemsa dark bands and yet are not quinacrine bright, the mechanisms of Q and G banding are not analogous. However, this does not negate other correlations drawn. The possible contribution of acid proteins in Giemsa banding is not disputed, since it is quite probable that acid and basic proteins are overlying DNA and each other. Since digestion with trypsin results in a progression of G-bands to C-bands to complete chromosome degradation, it must be concluded that the metaphase spreads showing "little or no banding" represent a relative lack of trypsin effect; this was confirmed by a test in the laboratory. The concept of a layering protein dissociation as a part of the Giemsa banding is probably valid. (12 refs.) - *A. C. Schenker.*

State Laboratory of Hygiene
University of Wisconsin
Madison, Wisconsin 53706

2543 Describing banded chromosomes. *Lancet,* 1(7799):358-359, 1973. (Editorial)

Chromosome banding techniques described are not necessarily alternatives but may be complementary, and full definition of a karyotype may require several of them. A report of the 1971 Paris conferences on standardization in human cytogenetics is concise and comprehensive. The Paris recommendations deal with the nomenclature, which depends on 4 techniques, each of which demonstrates a characteristic banding pattern. The Paris system states that the short arms (p) and the long arms (q) are divided into bands that may be dark or light depending on the technique; there are no interbands. The center points of certain striking features are taken as cytological landmarks which divide the chromosome arms in one to four regions; these are numbered outwards from the centromere. There are two versions of the nomenclature: the shorter is a simple modification of the Denver system; and the longer, which allows a detailed end-to-end description of the rearranged chromosomes, will be particularly useful in describing derived chromosomes in unbalanced karyotypes. Among the applications of these techniques (besides the discovery of new chromosome aberrations) is the new insight which study of banding patterns gives on chromosome structure. (13 refs.) - *A. C. Schenker.*

2544 MUTTON, DAVID E. Origin of the trisomic 21 chromosome. *Lancet,* 1(7796):375, 1973. (Letter)

Studies similar to those described by Robinson which demonstrated the value of heteromorphic quinacrine fluorescent variants in determining the meiotic error in Down's syndrome are described. One patient with Down's syndrome, born to a mother of 35, showed intense fluorescent satellites on two chromosomes 21. The mother had only one such variant chromosome and the father had none. Making the assumption described by Robinson, it is clear that nondisjunction occurred at maternal anaphase II, or alternatively at mitosis in the zygote. - *A. C. Schenker.*

Guy's Hospital Medical School
London SE1, England

2545 HARNDEN, D. G.; & O'RIORDAN, M. L. Down's syndrome and leukemia. *Lancet,* 1(7797):260-261, 1973. (Letter)

A study of childhood malignancies is presented to support the evidence that an association exists

between Down's syndrome and acute leukemia. Of 89 children with leukemia, 4 were found with abnormal chromosomes: 2 girls with acute leukemia had a 47,XX,G+ karyotype, and are clinically cases of Down's syndrome. It is assumed that the incidence of Down's syndrome is roughly 1 in 600 of all births; the finding of 2 cases in 89 children with leukemia is compatible with an increase of 12-15-fold in the incidence of leukemia in patients with Down's syndrome. The finding of 2 children with abnormal chromosomes in 87 cases of leukemia (excluding the 2 cases of Down's syndrome) does not support the high frequency figures reported by Borges (3 cases in 25). (3 refs.) - *A. C. Schenker.*

University of Birmingham
Birmingham B15 2TJ, England

2546 **FUJIMOTO, ATSUKO; EBBIN, ALLAN J.; & WILSON, MIRIAM G.** Down's syndrome and nonimmunological hydrops fetalis. *Lancet*, 1(7798):329, 1973. (Letter)

Two hydropic infants who had Down's syndrome with trisomy G are described; in both instances, the blood types of the mothers and the infants were A-positive and the direct Coombs test on the infants' blood was negative. The serological test for syphilis was negative in both. Although hydrops fetalis is most commonly associated with erythroblastosis, a significant number of hydropic infants are born without any evidence of blood-group incompatibility between mother and fetus. The association of Down's syndrome with nonimmunological hydrops fetalis might be looked for by other investigators. - *A. C. Schenker.*

1200 N. State Street
Los Angeles County-U.S.C.
Medical Center
Los Angeles, California 90033

2547 **ROBINSON, JACQUELINE A.** Origin of extra chromosome in trisomy 21. *Lancet*, 1(7795):131-133, 1973.

The origin of the extra chromosome or chromosomal material is described in patients with Down's syndrome: 12 with standard trisomy 21 and 3 with mutant translocation. Chromosome studies were carried out on peripheral blood lymphocytes, cultured and prepared by a modification of Hungerford's method. Cells from each individual (parents and child) were analyzed directly from the microscopic preparations. The variation in phenotype was found to be quite large: fluorescence of the short arms may vary from pale to intense, the size of the short arms from small to large; the stalk from neligible to long; and the satellites from nonexistent to large and from pale to intense. There were 5 cases which were shown to be due to maternal first meiotic nondisjunction. The maternal age effect on the incidence of Down's syndrome has led to the idea that nondisjunction in the mother is the most likely cause of trisomy 21, and the data presented indicate that first meiosis is the most common time for that nondisjunction. (14 refs.) - *A. C. Schenker.*

Medical Research Council Clinical
Unit
Western General Hospital
Edinburgh EH4 2XU, Scotland

2548 **LEE, STANLEY L.; & ROSNER, FRED.** Down's syndrome and acute leukemia. *Lancet*, 1(7794):110, 1973. (Letter)

An editorial quoting the incidence of acute leukemia in Down's syndrome erroneously quoted figures which were not representative of such incidence. What the report was intended to convey was that when children with Down's syndrome get leukemia they do in fact get the same kinds of leukemia (morphologically and clinically) as do normal children. Acute myelogenous leukemia is not the characteristic leukemia of Down's syndrome children. (5 refs.) - *A. C. Schenker.*

Jewish Hospital and Medical
Center of Brooklyn
Brooklyn, New York 11238

2549 **WALSHE, J. M.** Tutankhamun: Klinefelter's or Wilson's? *Lancet*, 1(7794):109-110, 1973. (Letter)

Reference is made to the comment by Weller that the statuette of the Pharaoh Tutankhamun has obvious breast development. It is pointed out that only one of the 4 statuettes in the British Museum exhibition showed this feature. However, all 4 show a sagging abdominal wall and flat feet. The association of 3 separate abnormalities certainly

suggests a genetic basis for Klinefelter's syndrome, which is not surprising in a royal line that officially practiced incest. Another possibility is that the gynecomastia is that of liver disease associated with a lax ascites and the slightly dystonic stance of Wilson's disease. - *A. C. Schenker.*

Department of Investigative
Medicine
Downing Street
Cambridge CB2 1QN, England

2550 **DE BAULT, L. E.; JOHNSTON, E.; & LOEFFELHOLZ, P.** Incidence of XYY and XXY individuals in a security hospital population. *Diseases of the Nervous System*, 33(9):590-593, 1972.

Adaptation of a quinacrine mustard fluorescence technique for visualization of banding patterns in metaphase chromosomes was achieved concomitantly with an investigation of the incidence of XXY and XYY chromosomal defects in 253 convicted felons at a state security medical inst whose offenses resulted from unusual and unacceptable patterns of behavior. Only 1 47,XYY and 2 47,XXY individuals were seen, their karyotypes being abnormal only in that they had an extra X or Y chromosome with no chromosomal or chromatid breaks, isochromosomes, inversions, translocations, or deletions. The findings were confirmed by the quinacrine mustard technique. (21 refs.) - *B. J. Grylack.*

Psychopathic Hospital
University of Iowa
Iowa City, Iowa 52240

2551 **KEDZIORA, J.; HUBNER, H.; KANSKI, M.; JESKE, J.; & LEYKO, W.** Efficiency of the glycolytic pathway in erythrocytes of children with Down's syndrome. *Pediatrics Research*, 6(1):10-17, 1972.

Some intermediates of the glycolytic pathway in acid soluble extracts of erythrocytes from children with Down's syndrome were studied to determine possible underlying mechanisms. Nine children with Down's syndrome and 6 healthy children were examined for blood morphology, hematocrit, adenine and guanine nucleotides, coenzymes, inorganic phosphates, and other intermediates. The results revealed a decrease in levels of adenosine 5'-triphosphate (ATP) and 2,3-diphosphoglyceric acid (2,3-DPG) and an increase in the levels of adenosine 5'-monophosphate (AMP), guanosine 5'-triphosphate (GTP), nicotinamide adenine dinucleotide (NAD), NAD phosphate (NADP), inorganic phosphate (Pi), and hexose diphosphate (HDP) in the children with Down's syndrome and trisomy G. The results suggest two kinds of mechanism which disturb the synthesis of ATP: an increased turnover of the pentose cycle in children with trisomy G as shown by the increase in NADP; and a partial inactivation of the enzymes which would explain the decrease in ATP. The results also show that there are biochemical differences between patients with trisomy G and those with unbalanced chromosomal translocation (2 siblings). This biochemical difference cannot be explained by a slight loss of genetic material when the centric fusion type of translocation occurs. (16 refs.) - *A. C. Schenker.*

University of Lodz
Lodz, Poland

2552 **HIGURASHI, MAKOTO; & CONEN, PATRICK E.** In vitro chromosomal radiosensitivity in patients and in carriers with abnormal non-Down's syndrome karyotypes. *Pediatrics Research*, 6(5):514-520, 1972.

The *in vitro* effects of radiation on cultured lymphocytes and fibroblasts from patients with various types of chromosomal abnormalities and from carriers with translocated chromosomes are reported and compared with effects found in normal control Ss. Lymphocytes and fibroblasts from 21 Ss were investigated: 5 children and 3 adults with normal karyotypes; 7 Ss with chromosomal abnormalities; and 6 carriers. The number of chromosomal breaks in cultures from patients with chromosomal abnormalities and from balanced translocation carriers was not significantly greater than that for control Ss. Peripheral blood samples and skin fibroblast cultures were irradiated with 10 and 100 rads; nonirradiated duplicate cultures were used as controls. After irradiation, the number of breaks/cell/rad in cultures from patients with chromosomal abnormalities and from balanced translocation carriers was significantly greater than that for controls. Another study showed that cells with abnormalities such as trisomy, deletions, and translocations all have

higher chromosomal radiosensitivity as measured by the frequency of chromosomal aberrations after 2 unit doses of gamma rays. (20 refs.) - *A. C. Schenker.*

Kyorin University School of
Medicine
Tokyo, Japan

2553 LUCAS, MARY; MULLARKEY, MARY; & ABDULLA, USAMA. Study of chromosomes in the newborn after ultrasonic fetal heart monitoring in labour. *British Medical Journal*, 3(5830):795-796, 1972.

The effect of continuous wave ultrasound was studied on the chromosomes of 24 newborn infants of women who had had a Sonicaid FM2 monitor applied to their abdomen in labor and a control group of 12 infants. The cultures were harvested after 2 days so that cells could be analyzed in the first mitosis following insonation. The average number of cells with an aberration did not vary between the 2 groups. The finding of 1 cell from an insonated infant containing 2 dicentric chromosomes and 2 acentric fragments was not considered significant. (17 refs.) - *B. J. Grylack.*

Galton Laboratory
University College
London N.W.1, England

2254 Management of postpubertal mongols. *British Medical Journal*, 3(5834):227, 1972.

The management of episodes of aggression linked with sexual curiosity in mongols is generally similar to that of like behavior in children of normal intelligence at the same stage of physical development. The penis and scrotum are underdeveloped and the testes undescended at birth in up to 50% of mongols, reduced sperm counts have been reported in the semen of adult mongols, and no case has been proven of a mongol's fathering a child. (5 refs.) - *B. J. Grylack.*

2555 LOTT, IRA T.; CHASE, THOMAS N.; & *MURPHY, DENNIS L. Down's syndrome: Transport, storage, and metabolism of serotonin in blood platelets. *Pediatrics Research*, 6(9):730-735, 1972.

The evaluation of aspects of serotonin (5HT) metabolism in the platelets of Down's syndrome patients as compared to normal controls is presented. The patients comprised 9 males and 5 females, ages 8-25 years, all living at home; control groups consisted of 12 nonsiblings (7 males, 5 females) of the patients and 9 nonsibling controls (5 males, 4 females), all matched for age. Uptake of 5HT was measured by incubation of platelet-rich plasma with ^{14}C-5-hydroxytryptamine creatinine sulfate and harvesting of the unsuspended platelets by centrifugation after 3- and 30-min periods of incubation. In other experiments ^{14}C-5HT was added directly to fresh platelet-rich plasma, sedimented by centrifugation, and after washing resuspended in either autologous plasma or in tris-phosphate buffer containg glucose and sodium citrate. After incubation, in both methods, the labeled amine was extracted and indentified by thin-layer chromatography. Levels of 5HT were measured fluorometrically. Endogenous 5HT content was reduced by 61% in the Down's syndrome as compared with sibling controls ($p < 0.001$) and by 68% in comparison to nonsibling controls ($p < 0.001$). The initial uptake of labeled 5HT was reduced by 35% in the Down's syndrome patients, which was significantly less than in either control group ($p < 0.05$). Mongols did not differ from normal Ss with respect to monoamine oxidase activity. The decreased transport of 5HT into blood platelets in Down's syndrome patients may explain the low serotonin blood levels. (31 refs.) - *A. C. Schenker.*

National Institutes of Health
Clinical Center
Bethesda, Maryland 20014

2556 DUNLAP, DICKSON B.; AUBRY, RICHARD; & LOURO, JOSE M. The occurrence of the 45,X Turner's syndrome in sisters. *Journal of Clinical Endocrinology and Metabolism*, 34(3):491-497, 1972.

The occurrence of a 45,X Turner's phenotype in 2 sisters of a sibship of 5 is reported because of its rarity. Both sisters revealed sexual infantilism and below average height increase. On the basis of an examination of metaphase plates, karyotypes were interpreted as 45,X in both patients. Both patients were evaluated for primary amenorrhea, one at age 17 and the other at age 19 years; both responded to cyclic estrogen therapy with subsequent increase in stature. Both sisters manifested normal

learning abilities, the second sister despite the need of a hearing aid. It is submitted that this familial ovarian dysgenesis is unlikely to be due to chance, even though the other siblings and both parents had normal phenotypes and karyotypes. A possible malfunction arising as a mutation in one of the parents' germ cell line may be responsible for the abnormality in this case. Other familial chromosome anomalies reported in the literature are discussed. (37 refs.) - *A. C. Schenker.*

VA Hospital
Medical Research Division
Augusta, Georgia 30904

2557 **LEHRKE, ROBERT.** A theory of X-linkage of major intellectual traits. *American Journal of Mental Deficiency*, 76(6):611-619, 1972.

A substantial amount of evidence exists in support of the theory that the genetic loci for major intellectual traits are on the X chromosome. Such a hypothesis of X-linkage would explain the observed greater variability of male intelligence. This feature has consistently shown up in numerous population studies, where the preponderance of males over females at both the superior and MR ends of the intelligence scale is a well-established phenomenon. Epidemiologic data, as well, tend to show a strong sex linkage in cases of familial retardation. These studies reveal a pattern of more frequent transmission of MR from mother to child than from father to child, and show a marked familial incidence of retardation in males. Collateral hypotheses in support of the basic X-linkage theory suggest that these intelligence genes on the X-chromosome relate particularly to verbal functioning and that the observed deficit is attributable to some abnormality in the CNS itself. Both these hypotheses find support in recent clinical data, which indicate additionally that cases where sex linkage is a factor compose approximately 25 to 50% of all MR. (33 refs.) - *N. Mize.*

Brainerd State Hospital
Brainerd, Minnesota 56401

2558 **ANASTASI, ANNE.** Four hypotheses with a dearth of data: Response to Lehrke's "A theory of X-Linkage of Major Intellectual Traits." *American Journal of Mental Deficiency*, 76(6):620-622, 1972.

The evidence cited by Lehrke in support of his theory that major genes relating to intelligence are located on the X chromosome is extremely meager. Much of the data crucially necessary to any adequate evaluation of his hypothesis is either misinterpreted, misleading, unavailable, or erroneously cited. In other instances, the data cited are irrelevant. Particularly damaging to this case is the almost complete lack of attention to the effect of cultural factors on sex differences in intelligence variability. Likewise, the significance of physical handicaps and of MR having a recognizable pathology is treated indifferently in the interpolation of data from one study to the next. Overall, the most obvious feature of this paper is that it is completely inadequate from a scientific point of view. (9 refs.) - *N. Mize.*

Fordham University
Bronx, NY 10458

2559 **NANCE, WALTER E.; & ENGEL, ERIC.** One X and four hypotheses: Response to Lehrke's "A Theory of X-Linkage of Major Intellectual Traits." *American Journal of Mental Deficiency*, 76(6):623-625, 1972.

Despite some rather glaring misinterpretations of statistics, Lehrke's paper on X-linked genes and intelligence performs a useful function in directing professional attention to the number of X-linked recessive syndromes associated with MR. Particularly questionable, though, is his interpretation of the data on the excess of males among the inst MR population. It should be clear that cultural and parental attitudes greatly influence the trends in hospital admissions, thereby making it impossible to generalize on this observation by suggesting that a true excess of MR males exists in reality. In other instances, the results of studies referred to in the paper have either been taken out of context or can as easily be turned around to argue against his own hypothesis. (9 refs.) - *N. Mize.*

Vanderbilt University School
of Medicine
Nashville, Tennessee 37203

2560 **LEHRKE, ROBERT.** Response to Dr. Anastasi and to the Drs. Nance and Engle. *American Journal of Mental Deficiency*, 76(6):626-631, 1972.

While my original discussion on the sex linkage of intellectual traits was no doubt weak in certain particulars, the objections and criticisms subsequently advanced by Anastasi, Nance, and Engle do not at all refute the essential hypothesis. In many instances the requested additional data and information on interpretation are available by referring to the cited references. Only a lack of space in the original article prohibited more lengthy explanations and more elaborate expositions of the supporting data. In any case, while it can be admitted that various of the arguments presented can be interpreted to produce a different emphasis, the evidence still warrants accepting this theory as a basis for further research. (22 refs.) - *N. Mize.*

Brainerd State Hospital
Brainerd, Minnesota 56401

2561 **HERRIOT, PETER.** The effect of order of labelling on the subjective organization and clustering of severely retarded adults. *American Journal of Mental Deficiency*, 76(6):632-638, 1972.

The effect of forced labeling on the subjective organization and on clustering of related items was compared in 20 adults with Down's syndrome and in 20 other nonmongoloid MR adults from the same inst, approximately matched for MA and CA. Two sets of free recall experiments, utilizing slides of 6 familiar objects, were conducted under 2 different conditions: labeling was forced either in the order of the previous recall or in random order. Each S participated in both experiments, conducted a week apart. As expected, the results indicate that sequential labeling in the order of previous recall increases subjective organization as compared to random order presentation. In the second experiment, an overall condition effect was found, with random order presentation resulting in more clustering than previous recall phase labeling. The results of manipulating input order are less clear-cut in this experiment, however, since the difference was evidenced only on Day 2 for the mongoloid Ss and only on Day 1 for the nonmongoloids. These variations are most likely attributable to the different sequential strategies characteristic of the 2 groups. (5 refs.) - *N. Mize.*

Hester Adrian Research Center
University of Manchester
Manchester, England

2562 **LEE, LYNDA G.; & JACKSON, JOHN F.** Diagnosis of Down's syndrome: clinical vs. laboratory. *Clinical Pediatrics*, 11(6):353-356, 1972.

Using a checklist of 25 frequently found signs in cases of Down's syndrome, physicians performing only a thorough examination on 150 patients referred for suspected mongolism were able to make the diagnosis successfully with a high degree of accuracy. Of the 150 children included in this study, 120 were subsequently confirmed by chromosome analysis to have Down's syndrome. A comparison of these findings shows that no patient exhibiting fewer than 5 signs from the checklist was cytologically confirmed to have 21 trisomy, while no patient with more than 12 signs was cytologically normal. While this procedure does not eliminate the need for chromosome analysis, it does represent a quick approach to a reasonably reliable diagnosis in those situations where immediate chromosome studies are impractical. (4 refs.) - *N. Mize.*

University of Mississippi Medical Center
Jackson, Mississippi 39216

2563 **COLOVER, JACK; LUCAS, MARY; COMLEY, J. A.; & ROE, A. M.** Neurological abnormalities in the 'cri-du-chat' syndrome. *Journal of Neurology, Neurosurgery, and Psychiatry*, 35(5):711-719, 1972.

The clinicial findings in a 6½-yr-old boy with cri-du-chat syndrome included a hoarse, cat-like cry, frequent choking, feeding difficulties, delayed milestones, hypotonia of the arms, ataxia of the lower limbs, intention tremor of the left hand, extensor left plantar response, and asymmetry of the larynx. Karyotype revealed a small deleted group B chromosome (46 XY, Bp-). Binet IQ at age 6½ was 91, and at age 7½, WISC score was 78 (V IQ 75, PIQ 87). Although verbal functioning appeared to be sophisticated, he was unable to deal with number problems. The ITPA subtest scores at age 7½ were: auditory reception, 43; auditory memory, 38; grammatic closure, 37; auditory associated, 34; verbal expression, 26; and visual reception, memory, association, 34; verbal expression, 26; and visual reception, memory, association, and closure 26, 24, 22, and 20, respectively (normal is 40). He learned to read and

attends school with low-ability children. The findings of feeding difficulties and the typical cat-like cry indicated neurological abnormalities of laryngeal function. As no abnormalities could be detected in the parents of the S, chromosome studies provided an accurate diagnosis and a reliable base for prognosis of future pregnancies. (36 refs.) - *V. J. Goldberg.*

Brook General Hospital
London, S. E. 18, England

2564 MIKKELSEN, MARGARETA; & STENE, J. The effect of maternal age on the incidence of Down's syndrome. *Humangenetik*, 16(2):141-146, 1972.

The incidence of Down's syndrome is fairly common in Europe, about 1-2/1,000 births. Factors which may affect the incidence of Down's syndrome include standards of diagnosis, degree of reporting, and ethnic influence. The role of maternal age was recognized even before chromosomal association was recognized as associated with the syndrome. Examination of the frequency of translocations in Down's syndrome from a previous survey by the author indicated that among the categories, sporadic, inherited, and not reported, those of a sporadic nature comprise the majority of the cases. A further breakdown of the sporadic cases according to age revealed that mothers <30 yr of age bore the largest percentages of Down's syndrome children. Statistics of young mothers who had previously given birth to Down's syndrome babies revealed a 2% recurrence rate. Noteworthy when population frequencies of this type are investigated is the age distribution of women in the study; a survey conducted by the author of the greater Copenhagen area displayed a marked tendency to shift to younger mothers in recent years. (27 refs.) - *K. Der.*

John F. Kennedy Institute
DK-Glostrup, Denmark

2565 BLUMENTHAL, I.; & VARIEND, M. S. Maternal urinary oestriol excretion and fetal chromosome abnormalities. *Lancet*, 2(7786):1084, 1972. (Letter)

A 39-year-old woman who had undergone a normal pregnancy until 34 weeks' gestation was found to have consistently low urinary estrogen levels and was delivered subsequently of a female infant with the typical features of the 17/18 trisomy syndrome, as confirmed by chromosomal analysis. Although the evidence seems to indicate that it is the underlying congenital anomaly which results in a defect of the fetoplacental endocrine system, the finding of normal adrenal glands in the present case was not consistent with involvement of the fetal pituitary/adrenal axis. - *B. J. Grylack.*

Jessop Hospital for Women
Sheffield S37RE, England

2566 GREGORY, LINDA; WILLIAMS, RALPH; & *THOMPSON, EILEEN. Leucocyte function in Down's syndrome and acute leukaemia. *Lancet*, 1(7765):1359, 1361, 1972.

Ten of 63 children with Down's syndrome and 6 of 25 children with acute leukemia were found, in a controlled study, to have a high frequency of partial leukocyte dysfunction against *Staphylococcus aureus*. Both the phagocytic and bactericidal capacity of the polymorphonuclear leukocyte were examined in an effort to determine the possible relationship between the tendency to both infections and leukemia frequently observed among Down's syndrome patients. In contrast to findings among the 39 normal children and adults serving as controls, the range of values for the leukocyte bactericidal capacity was significantly greater in children with Down's syndrome and leukemia. Since the degree of abnormality in both study groups is similar, the link with leukemia may be more than coincidental. The possibility of a common mechanism which would account for both complications should be further examined. (17 refs.) - *N. Mize.*

*Llandough Hospital
Glamorgan CF6 1XX, England

2567 LAPPALAINEN, J.; & KOUVALAINEN, K. High hematocrits in newborns with Down's syndrome. *Clinical Pediatrics*, 11(8):472-474, August 1972.

Routine blood examinations of newborn infants ill enough to be referred for hospitalization during the first week of life have identified an extremely high capillary hematocrit as characteristic of newborn infants with Down's syndrome. This associ-

ation has not been previously reported. Of the 31 Down's syndrome infants included in the study, 29 had definitely elevated hematocrits as measured in capillary blood samples from heel punctures. Additionally, these same infants had lower whole blood prothrombin values. Prophylactic doses of vitamin K for these cases were felt to be an inadvisable measure in the absence of hemorrhage, since the risk of thrombosis might well be aggravated by its administration. (6 refs.) - *N. Mize.*

University of Helsinki
Helsinki, Finland

2568 **BREG, ROY W.; MILLER, DOROTHY A.; ALLDERDICE, PENELOPE W.; & MILLER, ORLANDO J.** Identification of translocation chromosomes by quinacrine fluorescence. *American Journal of Diseases of Children*, 123(6):561-564, 1972.

A quinacrine fluorescence method for identifying chromosome anomalies in metaphase lymphocyte cultures involves staining for 6 min in 0.5% quinacrine dihydrochloride, 3 min rinsing in water, and mounting in Gomori's tromethamine (tris)-maleate buffer at pH 6.5. The quinacrine technique permits the identification of each chromosome and many specific chromosome regions, which was not possible with previous methods. (12 refs.) - *V. J. Goldberg.*

Southbury Training School
Southbury, Connecticut 06488

2569 **SCHERZ, ROBERT G.; FRAGA, JUAN R.; & REICHELDERFER, THOMAS E.** A typical example of 13-15 trisomy in a Negro boy. *Clinical Pediatrics*, 11(4):246-248, April 1972.

This case report of a Negro boy with the classical malformations of 13-15 trisomy is only the second ever reported for an American black infant. The child was born at 40 wks gestation to a 23-year-old mother and exhibited all of the multiple anomalies typical of this syndrome. Buccal smears revealed a male chromatin pattern. The child was hospitalized several times between birth and the age of 2 yrs and showed signs of severe MR and motor retardation. At age 2 yrs, he was found dead in his crib. The cause of this trisomy is presumed to be nondisjunction during meiosis. (9 refs.) - *N. Mize.*

Madigan General Hospital
Tacoma, Washington 98431

2570 **BREG, W. ROY; & MILLER, DOROTHY A.** Identification of translocation chromosomes by quinacrine fluorescence. *American Journal of Diseases of Children*, 123(6):561-564, 1972.

Use of quinacrine dihydrochloride fluorescence patterns in 6 cytogenetic studies has enabled investigators to clearly identify several reciprocal translocations which had previously either been poorly defined or undetectable when only traditional orcein-stained preparations were used. The karyotypes of 3 profoundly MR patients and of 3 mothers of MR children were simply and rapidly identified with this technique. All showed translocations of one kind or another. The quinacrine fluorescence method is extremely sensitive and permits the recognition of every chromosome in the normal complement, requires only a few cells, and allows increased accuracy, a factor which will be of particular importance to the prenatal diagnosis of chromosome disorders. In consideration of these findings, other methods would seem to be inadequate for current studies in clinical cytogenetics. (12 refs.) - *N. Mize.*

Southbury Training School
Southbury, Connecticut 06488

2571 **PETIT, P.; & ENGELS, J.** Low maternal oestriol excretion and congenital chromosome abnormalities. *Lancet*, 2(7784):970, 1972. (Letter)

Similar findings of low estriol excretion during late pregnancy were found in 2 women who later delivered infants with Edward's syndrome. This finding, combined with evidence indicating abnormally low estriol excretion in pregnancies resulting in infants with Down's syndrome, supports the hypothesis of a relationship between reduced estriol excretion and congenital (chromosomal) defects in the fetoplacental system. (1 ref.) - *B. J. Grylack.*

University of Brussels
B-1000 Brussels, Belgium

2572 **HOLMES, GRACE E.; & *TUCKER, VIRGINIA.** Oculo-cerebro-renal syndrome. *Clinical Pediatrics*, 11(2):119-124, 1972.

The identification of features consistent with the oculo-cerebro-renal syndrome in 6 male family members in 4 generations suggests that transmission occurred by means of an X-linked gene. The pedigree is particularly interesting in that all of the known clinical, anatomical, and biochemical variations of this disease are well demonstrated. In one of the 2 living relatives described at length, the delayed onset of hyperaminoaciduria was suggestive of a progressive renal tubular lesion. Otherwise, both children exhibited the classical signs of the OCR syndrome, including congenital cataracts, marked hypotonia, areflexia, and proteinuria. (21 refs.) - *N. Mize*.

*University of Kansas Medical Center
Kansas City, Kansas 66103

2573 **JORGENSEN, P. I.; & TROLLE, DYRE.** Low urinary oestriol excretion during pregnancy in women giving birth to infants with Down's syndrome. *Lancet*, 2(7781):782-784, 1972.

Of 12 pregnant women bearing infants with Down's syndrome among a total of 5,000 pregnant women seen over an 8-year period, 9 (75%) had abnormally low estriol excretion, as compared with 16% of controls. In 6 of these 9 cases, the pregnancies were uncomplicated. The weight of the placenta in the 9 cases was relatively low. In 7 of the 9 cases, there were no signs of intrauterine malnutrition. It was suggested that the cause of the reduced estriol excretion lies in congenital defects in the endocrine fetoplacental system, especially the fetal hypothalamus, pituitary, or adrenal cortex. (12 refs.) - *B. J. Grylack*.

University Department of Obstetrics and Gynaecology
Copenhagen, Denmark

MEDICAL ASPECTS—Miscellany

2574 **MEERS, DALE R.** Contributions of a ghetto culture to symptom formation. *Clinical Proceedings, Children's Hospital, National Medical Center*, 28(3):60-76, 1972.

Observational studies, initiated in ghetto schools in 1965, are summarized from the psychoanalytic viewpoint. The schools observed were located in an area whose residents are predominantly Negro; about 60% of all families in the area have at least one or more illegitimate children. This area also had about the highest crime rate in Washington, D. C. The first grade of school was selected for initial observation; a remedial class, selected from children who were designated as unable to use a curriculum, was observed. About 60% of this "slow learner" group came from one-parent homes, the mean number of children per family being more than 5. The impression of passivity as a defense was manifest in such groups; aggression seemed overcontrolled. The prevalence and severity of MR were the most striking observations in these classrooms; observation of classroom functioning proved inadequate to distinguish between possible cultural or psychopathological contributions to retarded functioning. Two children representative of such groups are discussed; both children had psychiatrically disturbed mothers. Few ghetto parents contribute models for identification with educational ideals; compounded with academic problems are daily experiences with instinctual trauma. Apathetic behavior in the so-called MR children appears to provide one form of psychological accommodation. (38 refs.) - *A. C. Schenker*.

Children's Hospital National Medical Center
Baltimore-District of Columbia Institute for Psychoanalysis
Baltimore, Maryland

2575 **MEERS, DALE R.** Contributions of a ghetto culture to symptom formation. *Clinical Proceedings, Children's Hospital National Medical Center*, 28(5):138-139, 1972. (Letter)

Reference is made to the editorial review of the article on ghetto culture and symptom formation by Noshpitz. There are at least two ambiguities in the original article which have been erroneously

interpreted by Noshpitz. He suggests that the sampling criteria were violated by selecting one child (for the analysis of a representative MR) who in Noshpitz's opinion was not MR and who was atypical with respect to violence. It is a fact that this child, at age 8, cannot yet manage his alphabet, although he appears competent in matters other than formal schooling. With respect to atypical aggressivity, this child appeared as passive as the other children. His assault on another child was pointed out in the original paper as having been reported by himself. (1 ref.) - *A. C. Schenker.*

Children's Hospital National Medical
Center
Baltimore, Maryland

2576 **HOLDEN, KENTON R.; & DEKABAN, ANATOLE S.** Neurological involvement in nevus unis lateris and nevus linearis sebaceus. *Neurology*, 22(9):879-887, 1972.

Two male children with nevus linearis sebaceus (NS) syndrome and a female child with the nevus unis lateris (NL) syndrome presented with well-documented neurological involvement. The male propositi had an extensive left-sided sebaceous nevus skin lesion, epilepsy, MR, and neurological signs indicative of left cerebral hemisphere involvement. In 1 of these children, the hemisphere involvement was associated with left choroidoretinal coloboma and a duplicated left collecting system. The proposita had had a typical NL skin lesion since birth. She also showed MR, was subject to epileptic attacks, and had focal epileptiform discharges in the EEG arising from the left frontoparietal region. Of 40 cases with the NL and NS syndromes in the literature, including the present 3 cases, 23 had nevus lateris, 16 had nevus linearis sebaceus, and 1 appeared to have signs of both; all NS skin lesions were noted at birth, while the NL skin lesions were observed at birth in 76%; MR and epilepsy were encountered in 17.4% and 13%, respectively, of patients with NL, whereas both these conditions were present in 60% of patients with NS; and there was a 20.5% incidence of neoplastic conditions for both cutaneous syndromes combined. The high incidence of associated neurological abnormalities and an increased risk for development of various neoplastic conditions in patients with both NL and NS justify the inclusion of these syndromes in the group of neurocutaneous dysgeneses. (22 refs.) - *B. J. Grylack.*

National Institute of Neurological
Diseases and Stroke
National Institues of Health
Bethesda, Maryland 20014

DEVELOPMENTAL ASPECTS—Physical

2577 **GRIFFITHS, MARGARET I.** Special handicaps: motor disability. In: Griffiths, Margaret I., ed. *The Young Retarded Child: Medical Aspects of Care.* Baltimore, Maryland, Williams & Wilkins, 1973, Chapter 10, p. 103-117.

Motor disorders most commonly interfering with a child's development are empirically divided into four groups: the floppy infant syndrome, cerebral palsies, progressive disorders of the central nervous system, and motor disorders associated with congenital abnormalities of the central nervous system. The floppy infant syndrome may be caused by disorders of the peripheral nervous system, disorders of the central nervous system, or by general disorders leading to muscular weakness rather than hypotonia. Cerebral palsies may result from insults to the child during the prenatal, perinatal, or postnatal period. Progressive neurological disorders are usually due to an inborn error of metabolism but also occasionally are the results of progressive encephalitis. Congenital anomalies of the central nervous system depend upon both genetic and environmental factors. - *C. Wares.*

University of Birmingham
Birmingham, England

2578 **SIMON, G. B.** Special handicaps: blindness and deafness. In: Griffiths, Margaret I., ed. *The Young Retarded Child: Medical Aspects of Care.* Baltimore, Maryland, Williams & Wilkins, 1973, Chapter 9, p. 98-102.

Varying degrees of the handicaps of blindness and deafness present diagnostic, assessment, and management problems, especially in MR children. The incidence for such handicaps is high in children, 1 in 5 having defects of vision or hearing and 1 in 20 being blind. Treatment and management for such children are especially important in augmenting the therapy and treatment for their mental handicaps. Parent guidance is especially helpful in directly aiding the child, since multiply handicapped children should be treated for the summation of their problems simultaneously rather than each one individually. Parents are thus a key ingredient in any program of therapy. Close follow-up and home guidance may be supplemented by special residential facilities which offer specialized training, therapy, and guidance. - *C. Wares.*

University of Birmingham
Birmingham, England

2579 **OSLER, DAVID C.; & *CRAWFORD, JOHN D.** Examination of the hypothesis of a critical weight at menarche in ambulatory and bedridden mentally retarded girls. *Pediatrics,* 51(4):675-679, 1973.

The age at menarche was determined in inst children to discover whether menarche occurred at the same critical body weight as in the normal population. The Ss comprised 44 patients, of whom 35 girls were ambulatory and the other 9 were bedridden. Age at menarche averaged 13.8 for all the Ss, with a range extending from 9.7-17.6 years. The mean age for the bedridden was lower than the ambulatory group; the bedridden girls also had a lesser weight than the ambulatory at the onset of menstruation. The data indicate that ambulatory MR girls in an inst setting reach menarche at a later date than do normals, but at the same mean weight and total body water as normals. The delay of menarche in the ambulatory MR girls might be a primary function of their brain disorders, but malnutrition might be a determinant factor. It is possible that in the bedridden girls, the factor of a lower metabolic rate is instrumental in creating the characteristic parameter for initiation of menstruation of 28 calories/kg/24hr, thus resulting in an early menarche. (28 refs.) - *A. C. Schenker.*

The Children's Service of
The Massachusetts General
Hospital
Boston, Massachusetts 02114

DEVELOPMENTAL ASPECTS—Mental

2580 **CLARKE, A. D. B.** Commentary on Kouchova's "Severe deprivation in twins: a case study." *Journal of Child Psychology and Psychiatry and Allied Disciplines,* 13(2):103-106, 1972.

The effects of malnutrition, severe cruelty, neglect, and isolation, as witnessed by the case of the Koluchova twins, agrees with previous incidents of this nature in the literature; characteristic effects include lack of speech, rachitis, and functioning at the imbecilic level. Although mental and physical development were greatly retarded at the time of discovery, deprivation for 5½yr beginning at 18mo of age did not relegate the Ss to permanent severe subnormal functioning. Theoretical aspects of perceptual and linguistic development are discussed in the light of the relatively rapid recovery which the twins experienced after and during treatment. Psychological experiences and their relationship to the learning process, in terms of reinforcement, cast considerable doubt upon theories which stress the prominence of early experiences on later growth. The extent and duration of reinforcement or lack of it afterwards is believed to be of greater significance than early learning itself. - *K. Der.*

The University of Hull
Hull, England

2581 **KOLUCHOVA, JARMILA.** Severe deprivation in twins: a case study. *Journal of Child Psychology and Psychiatry and Allied Disciplines,* 13(2):107-114, 1972.

A case history is presented of monozygotic twin boys who, for the first six years of life, were

confined to most abnormal conditions. After spending a considerable time in a children's home following their mother's death and other domestic complications, the boys were kept isolated from the outside world, living in a small unheated closet furnished with a polyethylene sheet for sleeping and some building bricks for toys. Denial of adequate food, fresh air, sunshine, and exercise combined with frequent physical abuse contributed to physical retarded development indicative of a 3-year-old at CA 6 yr.; walking proved difficult when the boys were moved from their parents and placed in kindergarten. During the time under state care the twins gradually overcame the timid and mistrustful attitude displayed towards other individuals and the surprise and horror in viewing everyday objects and activities. At the time of their discovery spontaneous speech in the twins was extremely poor; communication was achieved though primitive gestures, for speech did not appear to be the accustomed mode of expression. It was particularly noteworthy that the twins could not understand the meaning or function of pictures, a direct result of stimuli deprivation. MA was assessed at approx 3 yr when CA was 7 yr. Development under state and foster care has been rapid, raising the level of functioning of the Ss close to that of their peers. - *K. Der.*

Palacky University
Olomouc, Czechoslovakia

2582 **EAVES, L. J.; & JINKS, J. L.** Insignificance of evidence for differences in heritability of IQ between races and social classes. *Nature*, 240(5376):84-88, 1972.

Estimates of heritability from the available data on IQ are reexamined and qualitative and quantitative minimal requirements for such data are defined for estimates of heritability and of genetic, environmental, and interactive components of variation. Dr. Scarr-Salpatek's data are considered to fall short of the minimal requirements in that there is no complete classification of twin pairs into monozygotic and dizygotic. The data are reanalyzed in an analysis of variation of the z values in a linear model; the model includes, besides the overall mean value of z, the effects due to race, socioeconomic status (SES), and the difference between the same sex (SS) and opposite sex (OS) twins. The results of the reevaluation reveal that there is no significant overall difference between the correlations for SS and OS twins; that the interactions of the SS/OS difference with race and SES are not significant; and that there is no difference in the magnitude of a common environmental component between the races or the two social groupings. The only tenable conclusion is that there is a highly significant correlation between twins of all kinds for verbal IQ ($z = 0.597$, $P < 0.001$, $r = 0.54$). There is no evidence that this result has a genetic basis. (14 refs.) - *A. C. Schenker.*

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Birmingham B15 2TT, Great
Britain

2583 **LANGELEY, JAN; *DREW, CLIFFORD J.; & WATSON, CARRIE M.** Performance of retarded children on a liquid conservation task: Protocol objectivity and visual screening. *American Journal of Mental Deficiency*, 76(6):729-732, May 1972.

In evaluating the performance of 48 MR children (mean MA, 607; mean IQ, 50) on a liquid conservation concept task, MA was found to be the sole significant predictor of differences between MR and MR Ss. No significant differences in performance could be attributed to either visual screening or to the degree of scoring objectivity. These findings are at variance with those of other investigators and provide essentially no support for the claim that visual screening reduces the age of conservation development or that objectivity in scoring influences conservation scores on a Piagetian task. Also, contrary to expectations, few Ss actually attained conservation in this study. (8 refs.) - *N. Mize.*

*University of Utah
Salt Lake City, Utah 84112

2584 **HARGIS, CHARLES H.** A comparison of retarded and nonretarded children on the ability to use context in reading. *American Journal of Mental Deficiency*, 76(6):726-728, 1972.

The ability to use context clues in reading was compared between 15 MR children (IQ 55-70) and 15 MR children of similar CA, 10 to 12 years. Scoring on the cloze-treated passages employed in the testing, in which every fifth word was deleted, showed the MR Ss to have a significant deficiency

in their ability to use context in reading successfully even when each passage was individually adjusted to be of equivalent readability levels. As compared to the non-MR Ss, the MR group experienced significantly greater difficulty in supplying synonymous, grammatically correct words, while differences in the ability to supply exact words were not statistically significant. This variation is probably related to the differences in intellectual level between the groups and may, in part, reflect the more limited vocabulary characteristics of MR children. (12 refs.) - *N. Mize.*

University of Tennessee
Knoxville, Tennessee 37916

2585 **GOODSTEIN, H. A.; BESSANT, HELEN; THIBODEAU, GERARD; VITELLO, STAN; & VLAHAKOS, IRENE.** The effect of three variables on the verbal problem solving of educable mentally handicapped children. *American Journal of Mental Deficiency*, 76(6):703-709, 1972.

Verbal problem solving performance in EMR children at three MA levels, 7, 8, and 9 yrs, was investigated under experimental conditions. Of the 4 variables examined, the interaction of MA and the use of pictures as problem-solving aids was determined to have significant effect on performance. The presence of extraneous information and the use of superordinate set language had no significant effect on the children's ability to solve arithmetic word problems. Among the 3 groups of 6 children each included in the study, the performance of the MA 7 group was most markedly affected by the varying picture conditions, showing a significant deterioration when quantitative picture distractors were employed. Despite the small sample size, the findings can be interpreted as reflecting the immature problem-solving strategies employed by younger children. Additionally, they suggest that the span between MA 6 yrs. 8 mos, and 8 yrs, 0 mos is an important period for developing the ability to solve certain types of addition word problems. (13 refs.) - *N. Mize.*

University of Connecticut
Storrs, Connecticut 06258

2586 **WEBB, THOMAS.** Stereoscopic contour perception in mental retardation. *American Journal of Mental Deficiency*, 76(6):699-702, 1972.

No significant differences in the ability to recognize geometric designs produced by either stereoscopic or line contour were found in a comparison study of 70 EMR nonretarded Ss, aged 5, 8, 11, and 15 yrs. Both groups showed rapid and highly accurate recognition performance and exhibited a similar error pattern. Age factors had little effect upon performance. The consistently high performance level, generally, suggests that in mild forms of MR the cortical processing of binocular input is generally not distributed. (7 refs.) - *N. Mize.*

University of Pennsylvania
Philadelphia, Pa. 19104

2587 **MACMILLAN, DONALD L.** Paired-associate learning as a function of explicitness of mediational set by EMR and nonretarded children. *American Journal of Mental Deficiency*, 76(6):686-691, 1972.

The extent to which varying degrees of explicitness of a mediational set facilitate learning of paired-associate word lists was investigated in 3 groups of EMR and MA-matched nonretarded Ss. As measured both by trials to criterion and number of errors, the 2 study groups which used either an explicit or selfgenerated mediational strategy were superior in learning to the control group, which was required simply to name the objects in each of three 9-pair lists. On the transfer task, those Ss for whom an explicit mediating sentence was provided performed better than did either the control group or the group encouraged to generate its own sentences. No substantial differences between the EMR and nonretarded Ss were reflected in the variance analyses or in the quality of verbal mediators generated, a finding which tends to support the notion that MR children are not necessarily deficient in the ability to use verbal mediation. (11 refs.) - *N. Mize.*

University of California
Riverside, California 92502

2588 **HERTZIG, MARGARET E.; BIRCH, HERBERT G.; RICHARDSON, STEPHEN A.; & TIZARD, JACK.** Intellectual levels of school children severely malnourished

during the first two years of life. *Pediatrics*, 49(6):814-824, 1972.

Investigation of intellectual functioning at school age in 74 boys who had suffered severe malnutrition during the first 2 years of life and comparison with the functioning of age- and sex-matched siblings and unrelated Ss indicated that the previously malnourished Ss had lower levels of intelligence than their sibs and classmates at school age. No correlation was found between the intellectual level of cases and the ages at which the children were hospitalized for the treatment of severe malnutrition during the first 2 years of life. As anticipated, Full Scale, Verbal, and Performance IQ measures showed lowest scores for the previously malnourished Ss, highest scores for the unrelated Ss, and intermediate scores for the sibs. The differences between Full Scale and Verbal IQ scores for the Ss and their sibs were statistically significant ($p<0.025$). (34 refs.) - *B. J. Grylack.*

Rockland Children's Psychiatric
Hospital
Orangeburg, New York

2589 DENHOFF, ERIC; HAINSWORTH, PETER K.; & HAINSWORTH, MARIAN L. The child at risk for learning disorder. *Clinical Pediatrics*, 11(3):164-170, 1972.

A prospective study of 380 "culturally deprived" children, conducted by Brown University, indicates that major and minor neurologic signs observable at birth and in the first year are clearly associated with inefficient learning skills and poor school performance at age 7 yrs. Though only preliminary, these findings suggest that the development of an "Outcome Index," useful for indentifying the baby who is at risk for the later development of learning problems, is a realistic possibility. Initially, 5 specific stress-producing factors—respiratory distress syndrome, dysmaturity, low birthweight, high bilirubin levels, and hemolytic syndromes—were isolated and compared to 7-yr outcome ratings as measured by the WISC, IQ, WRAT, and MSSST. When considered individually, none of these stress factors related significantly to 7-yr status. Instead, a system of scored ratings of multiple outcome items was found to be the more useful indicator of psychoneurologic inefficiency in children. The potential importance of these findings to various environmental modification programs makes further followup studies, with larger samples, an important priority. (15 refs.) - *N. Mize.*

293 Governor St.
Providence, Rhode Island 02906

2590 GUTELIUS, MARGARET F.; KIRSCH, ARTHUR D.; MACDONALD, SALLY; BROOKS, MARION R.; MCERLEAN, TOBY; & NEWCOMB, CAROL. Promising results from a cognitive stimulation program in infancy. *Clinical Pediatrics*, 11(10):585-593, October 1972.

The preliminary evaluation of a minimal cognitive stimulation program for inner-city infants reports a mean IQ of 99.3 at 3 years of age in the experimental group, as compared to a mean of 91.2 for the control group. At birth the two series of 46 infants each were entirely comparable with respect to a multitude of variables. All were normal first-born, black infants of similar family background from the same low-income area of Washington, D.C. Mothers in the experimental group were regularly visited at home over a 3-year period by a public health nurse who counseled them on infant education and on how to provide appropriate sensory, motor, and language stimulation. These sessions supplemented regular pediatrician visits for well-baby care. In addition to significant differences in IQ, the experimental group at age 3 yrs showed more self confidence and ease in establishing a relationship with the tester and greater absorption in task, initiation of activity, and persistence as compared to controls. When looked at as a whole, success must in large part be attributed to the increased feeling of personal worth and self-confidence cultivated in the mothers throughout the program. While this program should not be seen as adequate for the eradication of culturally determined MR, its relatively low cost and the small amount of time actually invested recommend it as an initial step toward this goal. (28 refs.) - *N. Mize.*

Children's Hospital of
The District of Columbia
Washington, D. C. 20009

2591 How much of IQ is inherited? *Nature*, 240(5376):69, 1972.

As indicated by the fierce debate over the issue of how much of IQ is determined by genetic rather

than environmental considerations, scientists in the field of educational psychology must be careful not to make unfounded generalizations on the basis of the available data. Two years ago Jinks and Fuller published the results of an analysis of IQ data gathered on pairs of monozygous and dizygous twins reared together and concluded that the relative contributions of inheritance and environment could not be disentangled. Dr. Scarr-Salapatek, quarrying data for very large numbers of monozygous and dizygous twins from the Philadelphia school registers in a given month, was criticized by Jinks and another researcher for using a sample too small even to support the well-established conclusion that individual differences in intelligence are at least partially genetic in origin. - *B. J. Grylack.*

2592 **ISAACSON, ROBERT L.; & PERKINS, MARY A.** Delayed response performance of mentally retarded patients. *American Journal of Mental Deficiency*, 77(6):737-747, 1973.

Response strategies used in performance by retarded children and young adults, in comparison to normal controls, were studied in a simple observation of the S's responses to 2 discriminanda when all responses were reinforced and a simple discrimination problem. The Ss comprised 24 MR children and young adult patients, with IQs of 30-75; normal controls were 19 children with average or above normal IQs. After training in a discrimination task, Ss were given 10 preliminary trials with reinforcement; delayed response training was begun after the final trial of the discrimination task and those who learned this were advanced to the delayed response task. For those who learned the latter, the reward contingency was changed by reinforcing responses in predelay presentation. In the discrimination, delayed response, and delayed response reversal tasks, the majority of the retarded Ss acquired the problems as well as nonretarded Ss. The learning of the delayed response task appeared to be related to developmental level and reflected MA and CA for the nonretarded Ss. This was not true for the retarded Ss. For these Ss, MA only reached significant correlation with CA in the reversal of the delayed response problem. (27 refs.) - *A. C. Schenker.*

University of Florida
Gainesville, Florida 36201

2593 **OHWAKI, SONOKO; BRAHLEK, JAMES A.; & STAYTON, SAMUEL E.** Preference for vibratory and visual stimulation in mentally retarded children. *American Journal of Mental Deficiency*, 77(6):733-736, 1973.

On the assumption that the lower senses develop earlier than the higher senses, a study to demonstrate a shift in preference from vibratory to visual stimulation was conducted in retarded children as a function of mental age (MA). The Ss were 18 males and 12 females (CA 5-12 years), who received 10 forced-choice trials, 5 to a vibratory chair and 5 to a visual chair; after the forced-choice trials, 10 free-choice trials followed immediately. There was a significant difference in the mean frequency of vibratory choices among 3 groups examined (low, middle, and high MA): 8.0 for low, 5.0 for middle, and 4.2 for high MA. The greater preference of the low-MA group for vibratory stimulation supports the assumption of an earlier development of the lower senses than higher senses. (20 refs.) - *A. C. Schenker.*

Lynchburg Training School and Hospital
Lynchburg, Virginia 24505

2594 **FRIEDRICH, DOUGLAS; LIBKUMAN, TERRY; & THOMAS, ARTHUR.** Input deficit and stimulus enrichment: a replication-with-expansion. *American Journal of Mental Deficiency*, 77(6):687-693, 1973.

Gordon and Haywood's investigation, postulating the construct of input deficit, is examined critically and reanalyzed, and two new studies are added to substantiate the analysis. The variables analyzed include: (in inst MR Ss) etiology (cultural-familial or organic), age (late childhood and young adult), condition (similarities task and enriched similarities task), and order of tasks. The noninst Ss were similarly analyzed, except for age. Analysis of all the data reveals consistent findings pertinent to the earlier input deficit studies: significant Condition main effect, significant Order X Condition interaction, and nonsignificant Etiological Group X Condition interaction. From the 3 analyses, it appears that cultural-familial and organic MR Ss do not differ on similarities task

performance as would be predicted by the input deficit hypothesis. (7 refs.) - *A. C. Schenker.*

Central Michigan University
Mt. Pleasant, Michigan 48858

2595 **SCHMID-KITSIKIS, ELSA.** Piagetian theory and its approach to psychopathology. *American Journal of Mental Deficiency*, 77(6):694-705, 1973.

The Piagetian theory regarding the development of normal intelligence and his equilibrium model, based on the constant interaction between the subject and the objects and events which surround him, are discussed and some regulations which occur in the gradual equilibration are pointed out. Inhelder was able to show, in the context of the Piagetian perspective, that a certain analogy is possible between MR children and the egocentric mentality of younger children, on the level of a sort of false equilibrium. Current research is reviewed, within the framework of the Piagetian theory, in which 3 points are stressed: the acquisition of the first notions of conservation (matter, weight); the acquisition of class inclusion; and the difficulties in the establishment of simple spatial relations. Infantile psychoses are seen in the light of cognitive acquisitions. Regulations, as described in normal cognitive development, without disturbing affective factors influencing the equilibration process, are rarely observed in these subjects. The nature of the equilibration process in these subjects is complex and requires a deep knowledge of the mechanism underlying affective and cognitive development. (19 refs.) - *A. C. Schenker.*

University of Geneva
Geneva, Switzerland

2596 **KERSHNER, JOHN R.** Conservation of vertical-horizontal space perception in trainable retarded children. *American Journal of Mental Deficiency*, 77(6):710-716, 1973.

The spatial abilities of MR children were observed in relation to the concept that spatial conservation demands a reversible memory image and successful performance requires the correct sequential placement of objects in space. The Ss comprised 31 TMR children, whose CAs ranged from 8-10. The Ss were presented with various combinations of figure orientations and directional movements and were required to reproduce the space relations represented by the model on similar but rotated test fields; this ability to conserve multiple spatial relations is a right cerebral hemisphere function. It was found that the MR children showed a discrepancy in responding correctly to spatial direction and orientation. In Piaget's terms, the MR children's performance was characterized by perceptual dominance, irreversibility, transductive reasoning, and inability to decentrate. These children had a greater tendency than the non-MR children to fixate upon one aspect of the test field. (26 refs.) - *A. C. Schenker.*

The Ontario Institute for Studies
in Education
Toronto M5SIV6, Canada

2597 **DAS, J. P.** Reply of an eclectic to a developmentalist. *American Journal of Mental Deficiency*, 77(6):749-750, 1973.

A reply to a criticism of a study on MR children's cognitive processes and conclusions, previously reported, defends the original interpretation. The conclusion by Balla that the children were organically impaired is countered by the fact that none had obvious neurological signs of brain damage. Balla's inference of organic impairment from IQ scores in the high socioeconomic status (SES) Ss is untenable, particularly since the low SES Ss had a mean IQ of 65.53, and the difference in IQs was reflected on Memory for Design, especially since Memory for Design loads highly on a simultaneous-spatial processing factor. The tests used in the study are not tests for brain damage, as for example the test for Progressive Matrices. All the tests used can be described adequately by 2 orthogonal factors, simultaneous and successive processing. (6 refs.) - *A. C. Schenker.*

University of Alberta
Alberta, Canada

2598 **BALLA, DAVID.** Comment on Das' "Patterns of cognitive ability in nonretarded and retarded children." *American Journal of Mental Deficiency*, 77(6):748-749, 1973.

Das' interpretation of the performance of MR children, in a study where he concludes that a reexamination of the developmental approach to MR is called for, is questioned. From an examina-

tion of Das' data, in which he divided both MR and average IQ Ss into high and low socio-economic status (SES) subgroups, the high SES MR subgroup had a mean IQ of 68.63, which makes it probable that all high SES MR children were organically retarded. In addition, the experimental tasks used by Das are traditionally considered as indicators of organic brain damage in non-MR individuals. Thus, the Ss and criterion measurements are inappropriate for this study. (4 refs.) - *A. C. Schenker.*

Yale University
New Haven, Connecticut 06511

2599 **MCCONKEY, ROY; & HERRIOT, PETER.** The relationship between category labeling and sorting with retarded adults. *American Journal of Mental Deficiency*, 77(6):751-753, 1973.

The relationship between the sorting and labeling of categories was studied in 35 noninst Ss who were MR adults with mean CA of 24.49. Sorting, labeling, and category tests were administered using pictures. Ten Ss failed the sorting test completely, but all Ss gave some responses to the category test. There was a close correspondence between sorting and labeling of sort, and very few instances of categories that were sorted but not labeled. Noninst MR Ss show no evidence of having a verbal mediation deficiency; success or failure of detecting interitem relationships will determine the efficiency of sorting, but need not necessarily affect the verbalization of a category label. (5 refs.) - *A. C. Schenker.*

University of Manchester
Manchester, England

2600 **SPITZ, HERMAN H.; & LAFONTAINE, LOUISE.** The digit span of idiots savants. *American Journal of Mental Deficiency*, 77(6):757-759, 1973.

The digit span channel capacity was determined in idiots savants to discover how it compares to the normal range and that of the educable MRs. The raw score for Digits Foward on the Wechsler is that point where at least one of two digits spans of a given length are repeated in the correct order without error; this was used as the definition for digit span. The digit span of the idiots savants was significantly longer than that of the MRs of comparable age. One idiot savant had a digit span of 5, 5 had a digit span of 6, one of 7, and one of 9. These figures were within normal range, despite the idiots savants' lower IQs (48). (13 refs.) - *A. C. Schenker.*

E. R. Johnstone Training and Research Center
Bordentown, New Jersey 08505

2601 **FINCH, A. J., JR.; CHILDRESS, W. B.; & OLLENDICK, T. H.** Comparison of separately administered and abstracted WISC short forms with the full scale WISC. *American Journal of Mental Deficiency*, 77(6):755-756, 1973.

The relationship between scores on the Devereux Short Form of the Wechsler Intelligence Scale for children (WISC) and the full scale WISC was investigated, administered in counterbalanced order. Ss were 24 boys and 2 girls, diagnosed as MR. To avoid a sequential effect, a mixed design analysis of variance was performed with order of administration being the between S variable and test form being the within S variable. Correlations between short and full form were all significant ($p<.001$). The highest correlation was obtained between the abstracted Devereux short form and the fullscale WISC (administered consecutively) and the lowest correlation between the separately administered Devereux short form and the abstracted one. The results corroborate the usefulness of the Devereux short form of the WISC in evaluation of MR children. (3 refs.) - *A. C. Schenker.*

Virginia Treatment Center for Children
Richmond, Virginia 23201

2602 **GOODMAN, JOAN.** A case study of an "autistic-savant": mental function in the psychotic child with markedly discrepant abilities. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 13(4):267-278, 1972.

The phenomenon of the idiot savant with autistic behavioral patterns is interpreted as the developmental consequence of an early insensitivity to somatic stress. The child in question, originally observed at 6 2/3 years of age, was fascinated with dictionaries, phone books, almanacs, and the like,

and showed excellent long-term recall of their contents, but was defective in speech and speech comprehension and was unresponsive to people and his surroundings. Spatial discrimination and motor sequence memory were poor. Advanced skills in categorizing and processing analogies were coupled with incomprehension of syntax and practical cause-effect relationships. His superior memory for abstract data appeared due to a failure to forget, rather than to unusual rates of initial learning. These discrepancies suggest as etiology a deficiency in early motivation due to an inability to process somatic sensations, leading to passivity and distorted cognitive development of a kind that accommodates without assimilating. Hypothetically, the lack of a sense of inner status invests the world of print the child fixes upon with values of stability and permanence. (53 refs.) - *N. Jarvis.*

Northern California Regional Child
Development Center
Children's Hospital Medical Center
Oakland, California

DEVELOPMENTAL ASPECTS—Social and emotional

2603 **KOGAN, KATE L.; & TYLER, NANCY.** Mother-child interaction in young physically handicapped children. *American Journal of Mental Deficiency*, 77(5):492-497, 1973.

Social interaction patterns between preschool children with physical handicaps and their mothers were observed and compared with such interaction between MR and nonhandicapped children and their mothers. The Ss comprised 10 children with physical handicaps, 6 with MR, and 15 nonhandicapped Ss. The interaction protocol consisted of verbal and nonverbal communication records, compiled by trained observers outside a room equipped with a one-way mirror and microphone. The mothers of the physically handicapped children were found to be more controlling and warmer than the mothers of the nonclinic children, although the structure and organization of mother behaviors and attitudes differed only in degree. The physically handicapped children tended to play the role of passive participant. Mothers of the physically handicapped children behaved no differently than those of MR children, and the only behavioral difference between the children was that the physically handicapped were more assertive than the MR. It is suggested that the interactive style in the mother-child relationship in the case of the handicapped child is probably different than that of the nonhandicapped. (12 refs.) - *A. C. Schenker.*

University of Washington
Seattle, Washington 98195

2604 Influences on child development. *Lancet*, 2(7784):960, 1972.

Perhaps the most remarkable discovery made among numerous longitudinal studies is the variability in the pattern of individual development, some children progressing steadily and others showing large fluctuations from year to year. Evidence suggests that some of these variations are determined genetically, but it seems equally certain that much of the variation in growth rate is determined by environmental factors. While some aspects of early environment, such as nourishment within the first year, may undoubtedly be limiting, more attention should be concentrated on the later years and on improving the lot of the deprived child in every way throughout his development. (14 refs.) - *B. J. Grylack.*

2605 **KINGSLEY, RONALD F.; & BLIXT, SONYA L.** Differences of current-desired activities of accepted and rejected educable mentally retarded boys. *American Journal of Mental Deficiency*, 77(6):753-755, 1973.

Differential activity profiles of educable mentally retarded (EMR) boys were analyzed to discover those accepted or rejected by other EMR boys. An Interest Activities Inventory (IAI) questionnaire was submitted to boys enrolled in special classes, 65 of whom attended a school camping residential camp, CA being 11-14. The IAI was completed in the week prior to camp. Each boy was randomly assigned to one of the 7 cabins which housed 9-10 students. Sociometric data were gathered at the

end of the fourth day of camp. The responses made by the EMR boys on IAI items indicated that those who desired more interest and activities led the rejection status. EMR boys tended to have less expressed interest than their average ability peers. Such behavior may be associated with the EMR boys' reluctance to venture into the unfamiliar abstract activities and interests of children of comparable age. (10 refs.) - *A. C. Schenker.*

Kent State University
Kent, Ohio 44240

2606 **HALL, JUDY E.; MORRIS, HELEN L.; & BARKER, HARRY R.** Sexual knowledge and attitudes of mentally retarded adolescents. *American Journal of Mental Deficiency*, 77(6):706-709, 1973.

The MR adolescent's knowledge and attitudes regarding sex were studied in comparison to what the parent perceives such knowledge and attitudes to be, by the use of a questionnaire. Ss selected for the study were 61 adolescents, 56 of whom were diagnosed as MR and the remaining 5 as having learning disabilities. The same questionnaire was given to the adolescents and their parents; the latter were asked to answer the questions as they thought their children would answer them. The parent scores were significantly discrepant from the adolescent scores only on sex attitude. The amount of exposure to information on sexual topics did not correlate with all the test measures as expected; social class and the knowledge score by the adolescent were positively correlated; however, social class did not correlate with the attitude measures. The EMR lacked knowledge in certain areas: conception, contraception, and venereal disease. A need for education of both the parent and the adolescent in these areas is stressed. (7 refs.) - *A. C. Schenker.*

Center for Developmental and Learning Disorders
Birmingham, Alabama 35294

2607 **REES, H.M.N.** Special handicaps: disorders of communication. In: Griffiths, Margaret I., ed. *The Young Retarded Child: Medical Aspects of Care*. Baltimore, Maryland, Williams & Wilkins, 1973, Chapter 11, p. 118-133.

Children with noticeable disorders of communication, either in talking or in understanding language, may be referred to a variety of specialists in the medical field. Normal development of speech and language proceeds almost from birth, progressing through rather recognizable patterns and stages of development associated with specific age ranges. Grammatical language occurs at around 18 mos of age. Communication disorders may include primary disorders of speech development (stammering, aphonia, articulation disorders, dysarthria) or disorders of language development (disorders secondary to other defects such as brain damage, deafness, subnormality, social deprivation; or developmental language disorders such as aphasia or autism). Elective mutism is also a related problem. The multiple etiologic possibilities of disorders of communication pose a difficult problem for medical and paramedical personnel. - *C. Wares.*

Birmingham Regional Hospital Board
Birmingham, England

2608 **NEWMAN, HELEN G.; & DOBY, JOHN T.** Correlates of social competence among trainable mentally retarded children. *American Journal of Mental Deficiency*, 77(6):722-732, 1973.

The social competence of 110 children, classified as trainable mentally retarded (TMR, 30-50 IQ range), was evaluated using the variables of discrimination ability, basic knowledge, social behavior, self care, practical knowledge and skills, and communication skills. Social competence as measured on a Likert scale was found to be significantly related to CA, IQ, total school, teacher expectation, and interaction; there was also a positive correlation between organic and social competence. The results clearly indicated that trainable children, as well as normal children, become more adaptable with increased age and experience. The brain-damaged children, especially those designated as unspecified, are more socially adaptable than the specified brain-damaged or the Down's syndrome children. (25 refs.) - *A. C. Schenker.*

American Dental Association
Chicago, Illinois 60611

2609 **GATH, ANN.** The mental health of siblings of congenitally abnormal children. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 13(3):211-218, 1972.

A group of 36 school age siblings of 22 Down's syndrome children (D) and 35 siblings of 21 cleft palate/lip children (C) and 71 individually matched controls were compared to test the hypothesis that the siblings of congenitally abnormal children have more behavioral and emotional problems. Ritter behavioral scales completed by parents and teachers revealed no significant differences between D or C and their respective controls. Parents of 13 of 22 Down's children admitted moderate or severe management problems (limited social life, mobility, excessive expectations of normal children, or excessive attention to the affected child). Two of 21 parents of cleft palate/lip children reported moderate management problems, and 4 control parents reported difficulties (marital or school failure). (10 refs.) - *V. J. Goldberg.*

Warneford and Park Hospitals
Oxford, England

DEVELOPMENTAL ASPECTS—Psychodiagnostics

2610 **LEWIS, MICHAEL; & MCGURK, HARRY.** Evaluation of infant intelligence: infant intelligence scores—true or false? *Science*, 178(4066):1174-1177, 1972.

The assumptions that infant intelligence is a general, unitary capacity, that mental development can be enhanced by enriching the infant's experience in a few specific areas, and that infant intelligence scales reflect any improvement in competence that results from such experience, were tested in a longitudinal study. The Bayley Scales of Infant Development were administered to 20 infants at 3, 6, 9, 12, 18, and 24 mos, as was the object permanence scale from Escalona and Corman's Scales of Sensori-motor Development. At 24 mos, infants were given language comprehension and production tasks. The general conclusion based on the data was that there was no reliable relation between successive measures of infant intelligence during the first 24 mos of life. A similar picture emerged with respect to the measure of sensorimotor development. Although there was a regular increase in mean scores from one age to the next, high scores at an early age were not predictive of high scores later. Infant intelligence scales are considered unsuitable instruments for assessing the effects of specific intervention procedures, because infant intelligence is not a general, unitary trait, but is rather a composite of skills and abilities that are not necessarily covariant. (11 refs.) - *A. C. Schenker.*

2611 **TIPTON, ROBERT M.** Alternative cutoff criteria for selected WISC subtests as a function of level of performance. *American Journal of Mental Deficiency*, 76(6):732-734, May 1972.

The use of more stringent cutoff criteria on 3 of the standard WISC subtests has shown this alternative scoring procedure to be particularly appropriate for Ss functioning at a relatively low intellectual level. In comparison trials among 321 racially mixed students refereed for intellectual evaluation (mean full scale WISC IQ of 78.51), less variability in performance and fewer scoring errors resulted among Ss functioning at the lower intellectual levels when modified scoring criteria were employed in a rescoring of 2 of the subtests. While some investigators will resist using more stringent cutoff criteria, citing the need for standardized testing conditions, the psychological advantages of minimizing the failure set of these Ss should be carefully considered. (8 refs.) - *N. Mize.*

Virginia Commonwealth University
Richmond, Virginia 23220

2612 **KLEINBERG, WARREN; & O'CONNOR, PATRICIA A.** Appraising the effectiveness of a simple evaluational approach to problems of retardation and behavior in childhood. *Clinical Pediatrics*, 11(9):545-547, 1972.

The effectiveness of a simple University of Michigan evaluation program for childhood MR and behavior problems was assessed by comparing the extent to which parents understood and followed through on the recommendations noted in the patient's clinical record and by surveying

parent satisfaction or dissatisfaction with the evaluation process. The parents of all but two of the 20 cases, reviewed one year after the initial evaluation, reported that they were satisfied with clinic recommendations. Additionally, the parents' actual responses correspond very closely to the recorded treatment recommendations. Even though the sample is small, the results are encouraging and suggest that a clinical pediatrician and a clinical psychologist can adequately serve as the primary evaluation team for psychosocial clinic referrals. (7 refs.) - *N. Mize.*

University of Michigan Medical
Center
Ann Arbor, Michigan 48104

2613 GROTZ, R. THOMAS; HENDERSON, NORMAN D.; & KATZ, SIDNEY. A comparison of the functional and intellectual performance of phenylketonuric, anoxic, and Down's syndrome individuals. *American Journal of Mental Deficiency*, 76(6):710-717, 1972.

The functional behavior of 135 inst MR patients in 3 diagnostic categories—phenylketonuric, anoxic, and Down's syndrome—was evaluated on a scale originally developed for measuring the physical independence of elderly and chronically ill persons, the Index of Independence in Activities of Daily Living (ADL). Patients from 3 inst were evaluated by 2 experimenters as being functionally independent or dependent on a sliding scale which considered the regular attendant's assessment of behavior in feeding, continence, transferring, toileting, dressing, and bathing. Generally, scores on the ADL showed significant correlations with those on the Vineland Social Maturity Scale, but were at variance with other commonly used intelligence measures. PKU patients were found most dependent in performing the 6 ADL skills and least capable intellectually. SS with Down's syndrome were the least dependent functionally and of intermediate intelligence, while those with anoxia were shown to be most intelligent and of intermediate functional status. (23 refs.) - *N. Mize.*

Case Western Reserve School of
Medicine
Cleveland, Ohio 44106

2614 MILLER, MARTIN B.; & GELLER, DANIEL. Curiosity in retarded children: sensitivity to intrinsic and extrinsic reinforcement. *American Journal of Mental Deficiency*, 76(6):668-679, 1972.

In a departure from previous studies which involved mostly older patients, 50 EMR children (IQ 50-75) from 5 different primary and intermediate-level classes were tested for curiosity behavior. In an effort to modify their original curiosity behavior, determined by their choices from among a series of briefly exposed stimulus sets which varied along a 3-point complexity continuum, Ss were assigned to complete a puzzle under differing reinforcement conditions. The results were later analyzed for the stimulus triads in terms of latency to response, duration of response, consistency across items, sex, and age. In line with the original hypothesis, it was found that both intrinsic reinforcement factors (where Ss were interrupted before puzzle completion) and extrinsic factors (money rewards) differentially affected curiosity behavior, with both of these reinforced groups showing the highest post-puzzle curiosity scores. Overall, these results support the contention that curiosity behavior in MR persons is modifiable and can be brought under social control. (23 refs.) - *N. Mize.*

Studies in Nonverbal Behavior
San Francisco, California 94122

2615 OVERTON, G. WILLIAM; & *SCOTT, KEITH G. Automated and manual intelligence testing: Data on parallel forms of the Peabody Picture Vocabulary Test. *American Journal of Mental Deficiency*, 76(6):639-643, 1972.

Scores on the A and B forms of the Peabody Picture Vocabulary Test were compared under conditions of manual and automated presentation in an immediate test-retest program. Order of testing was counter-balanced. The manual testing procedure was conducted by the same male psychologist, while the automated technique utilized a visual display apparatus which has been previously described. Ss were 240 inst MR patients, representing a typical age and IQ spectrum. Essentially the same scores resulted under either manual or automated testing conditions, with a correlation rate of .91 to .94. Significantly lower scores under both conditions were typical of Form B. No practice effects were evident for either test or mode of presentation. Overall, these results clearly demonstrate the feasibility of using

automated tests with MR Ss. Since such a procedure holds many advantages for the psychologist, time-saving and otherwise, further research to refine this technique would seem to be warranted. (6 refs.) - *N. Mize.*

*University of Illinois
Champaign, Illinois 61820

2616 U.S. Bureau of Education for the Handicapped. *A comparison of conceptual strategies for grouping and remembering employed by educable mentally retarded and non-retarded children.* Riegel, R. Hunt; & Taylor, Arthur M. Research, Development, and Demonstration Center in Education of Handicapped Children, Minnesota University, Minneapolis, 1973, 28 p. [Research Report No. 46.] (Abstract)

The Sampling Organization and Recall Through Strategies (SORTS) test was administered to 87 EMR children (mean CA 97 months, mean IQ 70) and 31 non MR second-grade children to determine their characteristic grouping responses, the effects of various organizational strategies on recall and mnemonic organization, and the implications of the organizational strategies approach for classroom instruction. Sorting responses were categorized as syncretic strategies (level 1), perceptual strategies (level 2), low associative strategies (level 3), and superordinate and categorical strategies (level 4). In the third sort of the SORTS test, 13% of EMR Ss sorted the items into groupings classified as associative or better, as compared with 55% of nonMRs. NonMRs remembered nearly 4 items more than EMRs on an average. EMR children who had grouped associatively showed significant correlations between recall and clustering, which were not observed for the nonMR sample. - *B. J. Grylack.*

Research, Development, and
Demonstration Center in Education
of Handicapped Children
Minnesota University
Minneapolis, Minnesota

TREATMENT AND TRAINING ASPECTS—Educational

2617 **MCIVOR, WILLIAM B.** Evaluation of a strategy-oriented training program on the verbal abstraction performance of EMRs. *American Journal of Mental Deficiency*, 76(6):652-657, 1972.

Hypothesis-testing strategy training has proven superior to paired-associate training in preparing a group of inst EMR adolescents to apply thinking strategies to solve conceptual problems. Two paired experimental groups of 25 Ss each took part in this study. Both groups were trained for 5 days in 45-minute sessions using one of the 2 strategies for solving a verbal abstraction task. Unlike the paired associate group, which did not generalize training performance to the transfer materials, the hypothesis strategy group was able to use a learned approach to problem solving to determine the compatibility of a specific response (concept) with known data (triad). This finding is of major importance to the special education field and would seem to demonstrate rather conclusively the superiority of the hypothesis-testing strategy as a conceptual operation for MR individuals. (11 refs.) - *N. Mize.*

Special Education
Leonia, N. J. 07605

2618 North Carolina. State Department of Public Instruction, Division for Exceptional Children. *Career opportunities in teaching exceptional children.* Ramos, Pearle R. Raleigh, North Carolina, 1971, 29 p. (Abstract)

Special education career opportunities and professional training in universities are offered in North Carolina. Statistics on physically impaired, speech impaired, hearing impaired, visually impaired, learning disabled, emotionally disturbed, EMR, TMR, and gifted and talented individuals in North Carolina provide a comparison of the number of handicapped in the state with the number currently being served professionally. - *B. J. Grylack.*

North Carolina State Department of
Public Instruction
Division for Exceptional Children
Raleigh, North Carolina

2619 **FUNK, KERRI L.; & TSENG, M. S.** Effects of classification exposure upon numerical achievement of educable mentally retarded children. Paper presented at the 1973 Annual Meeting of the American Educational Research Association, New Orleans, February 27, 1973, 12 p. (Abstract)

Two groups of 32 EMR children (CA range 7 to 14 years) were compared with respect to their arithmetic and classification performance attributable to the presence or absence of a 4½-week exposure to classification tasks. The randomized block pretest-posttest design was used. Arithmetic posttest scores covaried significantly with arithmetic pretest scores and classification pretest scores, and classification posttest scores covaried significantly with CA and classification pretest scores. Experimental Ss demonstrated significantly better posttest performance on arithmetic and classification than the control group, an indication of the benefit derived from the classification exposure treatment. - *B. J. Grylack.*

2620 **BOAZ, P. D.** Feasibility of training mothers of the mental retardates in a day-care centre. Final Report. Bala Vihar, Kilpauk, India, 1971, 120 p. (Abstract)

MR children participated in a day care program while their mothers were trained through observation, lectures and films, and professional counseling. The children showed marked progress in various areas of activity after 6 months of training, as compared with a group whose mothers did not participate. The control group caught up when given an extra 12 months of training, but their learning deteriorated more quickly. A third group of children who attended for a 12-month period with their mothers showed no significant additional changes after the first 6 months. Mothers' attitudes improved significantly as a result of training. - *B. J. Grylack.*

2621 Ohio. State Department of Education, Division of Special Education. *Guidelines work-study phase of E.M.R. programs.* New, Frank E. Columbus, Ohio, 1972, 37 p. (Abstract)

Administrative guidelines derived from analysis of the practices and policies of work study programs for EMRs in high schools in Ohio are presented for the areas of program development, administrative involvement, criteria for selection of program coordinator, funding, extended summer services, and cooperation among programs. Different phases of work experience programs allow students to explore possible vocational choices, to be trained in a particular area, and to prepare for the adult working world through workshop or community placement. The work study coordinator plays a significant role within the program. - *B. J. Grylack.*

Ohio State Department of Education
Division of Special Education
Columbus, Ohio

2622 Ohio. State Department of Education, Division of Special Education. *Ohio's program for the education of the handicapped.* Interim report. Columbus, Ohio, 1973, 36 p. (Abstract)

The interim report on a comprehensive plan for the education of handicapped in Ohio places Subcommittee Senate Bill 405 in historical perspective, discusses its provisions and plans for its implementation, and outlines the present status and projected needs of programs for the handicapped. Preliminary recommendations are made concerning such issues as interdistrict cooperation, transfers for TMR children, early assistance, new special education units, and vocational opportunities for the handicapped. - *B. J. Grylack.*

Ohio State Department of Education
Division of Special Education
Columbus, Ohio

2623 U.S. Education Office. *Handicapped children in the regular classroom.* Fountain Valley School District, California, 1972, 26 p. (Abstract)

Sixty EMR and 30 educationally handicapped elementary school children were placed in regular classrooms to determine whether they could be educated effectively in these settings. Regular classroom teachers attempted to help handicapped students to feel that they were valuable members of the class. EMR's made an average of 9 months' growth in reading and 12 months' growth in mathematics achievement, while educationally handicapped Ss made an average of 11 months' and 12 months' growth, respectively, in these

areas. The Osgood Semantic Differential Scale showed no distinction in teachers' overall perception of handicapped versus nonhandicapped students. More educationally handicapped children were shown by 2 measuring instruments to have reached criterion levels than EMRs. - *B. J. Grylack.*

Fountain Valley School District
California

2624 Florida. State Department of Education. *Attending behavior: skills for teaching exceptional children. Teacher handbook. An inservice training program for exceptional child educators. EDUCOURSE I.* Curricula Improvement Center, Punta Gorda, Florida, 1972, 200 p. (Abstract)

The teacher handbook is presented for EDUCOURSE I, a program designed to increase attending behaviors of EMR students by instruction teachers in behavior modification techniques. Within the inservice course, 4 instructional sequences consider assessment of interfering behaviors, eliciting of attending behaviors, use of teacher attention to modify behavior, and establishment of a reinforcement system. The handbook provides considerable space for responses by the teacher. - *B. J. Grylack.*

Curricula Improvement Center
Punta Gorda, Florida

2625 U.S. Bureau of Education for the Handicapped. *Educational development and utilization of a composite approach to teaching the exceptional.* Curricula Improvement Center, Punta Gorda, Florida, 1972, 28 p. (Abstract)

Project EDUCATE is an inservice program designed to teach behavior modification techniques to 19 special education teachers and thus to reduce the occurrence of inattending behaviors in 400 EMR students. EDUCOURSE I consists of a teacher handbook presenting the theoretical basis of the course and containing lesson plan aids for microteach lessons and 4 videotaped model lessons. Significant achievement of the project objective was made by the teachers in the program. - *B. J. Grylack.*

Curricula Improvement Center
Punta Gorda, Florida

TREATMENT AND TRAINING ASPECTS—Psychosocial

2626 **BRY, PETER M.; & *NAWAS, M. MIKE.** Is reinforcement necessary for the development of a generalized imitation operant in severely and profoundly retarded children? *American Journal of Mental Deficiency*, 76(6):658-667, 1972.

In a series of experiments with 2 SMR and 2 PMR inst boys, reinforcement, along the lines of the stimulus-response model, was found to be a necessary condition for the development of generalized imitative behavior in children who did not previously imitate. In the absence of extrinsic reinforcement, no generalized imitative behavior developed. Despite some reservations concerning the Ss' actual nonimitative history and possible discrepancies in the consistency of attention to the model conducting the experiment, the results tend to favor strongly the stimulus-response pattern as a paradigm for imitative behavior. (11 refs.) - *N. Mize.*

*Indiana State University
Terre Haute, Indiana 47809

2627 **WOLFENSBERGER, WOLF.** Normalizing activation for the profoundly retarded and/or multiply handicapped. In: Wolfensberger, Wolf; Nijre, Bengt; Olshansky, Simon; Perske, Robert; & Roos, Philip. *The Principle of Normalization in Human Services.* Toronto, Canada, National Institute on Mental Retardation, 1972, Chapter 9, p. 122-135.

A frontier of treatment for the PMR and/or multiply handicapped person is the therapy of activation. Normalizing activation as developed by the Scandinavians refers to the involvement of persons in meaningful activities and implies motor involvement and mobility. There has been a fatalistic acceptance of inactivity and high mortality rates in MR insts and residences which is

unnecessary, according to the Scandinavian experience. Scandinavian insts encourage ambulation, mobility, and normalizing activities for patients and achieve high rates of success in normalization. It is proposed that their success be extended to the goal of abolition of immobility and nonambulation of MR and/or handicapped persons. Activation may be achieved by physical therapy, movement-oriented educational curriculum, work emphasis on younger patients, operant shaping, developmental materials, environments, and role perceptions; and positive interrelationship between activating measures. Some current activation interest is being shown in the areas of physical fitness of the MR, movement-mediated development of MR or handicapped persons, and attention to physical therapy and orthopedic needs of MR. It is hoped that activation will be implemented as a policy complementary to normalization. - *C. Wares.*

National Institute on Mental Retardation
Toronto, Canada

2628 **WOLFENSBERGER, WOLF.** Meeting the socio-sexual needs of severely impaired adults. In: Wolfensberger, Wolf; Nirje, Bengt; Olshansky, Simon; Perske, Robert; & Roos, Philip. *The Principle of Normalization in Human Services.* Toronto, Canada, National Institute on Mental Retardation, 1972, Chapter 12, p. 164-174.

Matter of fact acceptance of the sociosexual needs of MR adults and open practice of fulfilling such needs is common in Scandinavia. Such sexuality by North American standards is disturbing for reasons of eugenic traditions, fear of inadequate parenthood, perceptions of MR persons as nonhuman, egocentric concepts of sociosexual relationships and marriage, and religious-theological objections. With regard to North American culture, a useful reorientation is possible which would utilize some good features of a nonhypocritical approach toward sexuality while yet observing general cultural mores. A reassessment of sexual normalization is needed. - *C. Wares.*

National Institute on Mental Retardation
Toronto, Canada

2629 **BLINDERT, H. DIETER.** Strategies for the sequential and consequential arrangement of school-appropriate behaviors: the establishment of school-appropriate behaviors in normal, retarded and handicapped children through the application of operant tactics. Paper presented at the 1973 Annual Meeting of the American Educational Research Association, New Orleans, March 1973, 15 p. (Abstract)

Twenty MR children were enrolled in a special training program designed to increase their school-appropriate behaviors by means of the sequential and consequential arrangement of teaching objectives and procedures. The behavioral repertoire described by a hierarchy of 30 achievement levels appeared to be comparable to performances required of a normal child entering a standard first-grade class. Through participation in a total of 406 10-minute sessions, the Ss attained a total teaching time of 51 hours and 24 minutes. A total of 12,817 interactions between Ss and student trainees was used to establish the achievement levels. - *B. J. Grylack.*

2630 **NIRJE, BENGT.** The right to self-determination. In: Wolfensberger, Wolf; Nirje, Bengt; Olshansky, Simon; Perske, Robert; & Roos, Philip. *The Principle of Normalization in Human Services.* Toronto, Canada, National Institute on Mental Retardation, 1972, Chapter 13, p. 176-193.

A major facet of the normalization principle is to ensure respect for and self-determination of the handicapped person. Self-assertion by the handicapped is often feared in qualitative terms, but their experiences are formative of their specific needs in self-determination and should not be denied. Social training for MR handicapped persons enhances their capability for self-determination, such as participation in community experiences courses, social clubs, and training in parliamentary procedures. The Malmo congress of the MR (Sweden) was a historic step in progress in MR self-determination. Self-directing groups of the handicapped are necessarily segregating, but their objectives are integrative. Various forms of such groups may be useful, depending on the constitution and objectives of each group. Self-determination for the MR is seen as a test case for the self-determination of other socially devalued groups. - *C. Wares.*

Mental Retardation Services Branch
Ontario Government
Toronto, Canada

2631 **PERSKE, ROBERT.** The dignity of risk. In: Wolfensberger, Wolf; Nirje, Bengt; Olshansky, Simon; Perske, Robert; & Roos, Philip. *The Principle of Normalization in Human Services.* Toronto, Canada, National Institute on Mental Retardation, 1972, Chapter 14, p. 194-200.

New attitudes toward risk and the integration of the handicapped into society have developed in Scandinavia, based on the developmental potential of dignity for handicapped persons. Risk-taking experiences for the handicapped are being programmed as therapy in Scandinavia, including various community experiences, industry and work situations, heterosexual relationships, and building design normalization. The Scandinavian attitude toward risk for the handicapped is fully applicable to North American experience once the realization of the dignity of risk is accomplished. - *C. Wares.*

Greater Omaha Association for Retarded Children in Nebraska
Omaha, Nebraska

2632 **WOLFENSBERGER, WOLF.** Dignity and risk: a further reflection. In: Wolfensberger, Wolf; Nirje, Bengt; Olshansky, Simon; Perske, Robert; & Roos, Philip. *The Principle of Normalization in Human Services.* Toronto, Canada, National Institute on Mental Retardation, 1972, Chapter 15, p. 202-205.

There is dignity in being allowed to live normally as far as possible, even though the normal conditions of life may be more risky than inst or sheltered existence. It is dehumanizing to remove all danger from the lives of MR and handicapped persons. The story of an MR youth who gave his life in attempting to rescue his brother from a fire and interpersonal reactions to the incidents of the story offer proof of the value of such normalization. - *C. Wares.*

National Institute on Mental Retardation
Toronto, Canada

TREATMENT AND TRAINING ASPECTS—Occupational

2633 **OLSHANSKY, SIMON.** Changing vocational behavior through normalization. In: Wolfensberger, Wolf; Nirje, Bengt; Olshansky, Simon; Perske, Robert; & Roos, Philip. *The Principle of Normalization in Human Services.* Toronto, Canada, National Institute on Mental Retardation, 1972, Chapter 11, p. 150-163.

Human services agencies and inst have the intention of changing human behavior of their clients so that the person can function better in society. Normalization as a behavior modification methodology is criticized for its inattention to pathology, its "overrated expectations," its attention to experience, and its innovative newness. In using a workshop model as a medium for normalization, experience is seen as of paramount importance. Work in itself is seen as a normalizing experience, and substantial successes may be achieved with appropriate personnel selection and assistance in job placement after workshop tenure and training. - *C. Wares.*

Community Workshops
Boston, Massachusetts

2634 **BROLIN, DONN.** Value of rehabilitation services and correlates of vocational success with the mentally retarded. *American Journal of Mental Deficiency*, 76(6):644-651, 1972.

The efficacy of follow-up rehabilitation services for the MR, after a comprehensive initial diagnostic evaluation, and the relative importance of selected variables in the attainment of vocational success were investigated in 193 former clients of the Development Evaluation Center in Madison, Wisc. Ss, generally representative of more complicated MR cases, ranged in age from 18 to 54 yrs

and had IQs from 40 to 89. Three independent professional raters, none of whom were aware of the DEC's predictions of the client's vocational potential or of client outcome, evaluated the adequacy of vocational services based on center records and follow-up questionnaires. Overall, rater analysis judged 131 to be receiving adequate services and 62, inadequate services. In evaluating the correlates of vocational success, significant differences in the importance of variables were found between males and females. Chi-square analysis of client outcome, generally, found it to be significantly related to a number of client, family, community, and agency variables. Overall, the study upholds the value of rehabilitation services for the MR, especially males, but cautions that over half of those evaluated were either not attaining their vocational potential or had not received adequate rehabilitation services. (6 refs.) - *N. Mize.*

Stout State University
Menomonie, Wisc. 54751

2635 New Jersey. State Department of Education, Division of Vocational Education. *A pilot program, occupational education for students with special needs*. Beliveau, Joseph E. Union Township Board of Education, New Jersey, 1970, 34 p. (Abstract)

The Occupational Conditioning Center Program is a vocational education program designed to teach proper work attitudes and basic industrial skills to SMR individuals. Attainment of program goals is achieved through the use of an industrial time clock, simple assembly lines, and audio-visual aids, and by drilling students in safety skills. Completion of the program is followed by referral of students to sheltered workshop or competitive employment situations. Review of the program's first year appears to indicate that preemployment training has resulted in a smoother and more successful transition into the working force for the 20 TMR or EMR participants. - *B. J. Grylack.*

Union Township Board of Education
New Jersey

2636 KARAN, ORV C.; & GARDNER, WILLIAM I. Vocational rehabilitation practices: a behavioral analysis. *Rehabilitation Literature*, 34(10):290-298, 1973.

The process of vocational rehabilitation is described from the viewpoint of the counselor. His decisions may be of a program nature (general or specific) or of a treatment nature. General program decisions deal with acceptance of handicapped individuals as rehabilitation clients and establishing financial need. Specific program decisions deal with placement in a sheltered workshop and on the job training. General treatment decisions provide a well-structured environment and encourage social interaction with peers, and specific treatment decisions deal with encouragement by praise when the client asserts himself, and fining the client when he exhibits disruptive behavior. The rehabilitation counselor offers his services to clients whose handicapping condition occurred prior to work experience and to others whose disability prevents them from returning to a previous occupation. It is the counselor's responsibility to explain the various treatment decisions as well as the conceptual framework within which the plan is to be carried out. (37 refs.) - *A. C. Schenker.*

2637 CLARK, ALICE T. No "open sesames" in rural rehabilitation. *Rehabilitation Literature*, 34(7):207-209, 223, 1973.

In a 2-year study at the Opportunity Training Center of MR adults in rural North Dakota, a correlation was attempted between 27 initial testing, interview, and evaluation variables on 3 Indian and 37 Caucasian MR adults (CA range 16 to 53 years) and their ultimate job performance. Not one of the correlations between placement success measures and antecedent evaluations was significant, and there appeared to be no relationship between measures of IQ, school skill, personality, or biographical data and ultimate community and vocational adjustment. The 13 students who dropped out of the program prior to the completion of their year of training or who returned home shortly after the completion of their year were not significantly different from the rest of the sample on any measured variable. The 26 clients who were judged successfully placed at the end of the training program were not significantly different from the group judged unsuccessful. (14 refs.) - *B. J. Grylack.*

University of North Dakota
Grand Forks, North Dakota 58201

TREATMENT AND TRAINING ASPECTS—Therapy

2638 **SLOOP, E. WAYNE; & KENNEDY, WALLACE A.** Institutionalized retarded nocturnal enuretics treated by a conditioning technique. *American Journal of Mental Deficiency*, 77(6):717-721, 1973.

The treatment of enuretics by the conditioning technique of an electric buzzer warning device triggered by urinating in bed was applied to inst MR Ss, and the results obtained were compared to a control group. Twenty-one pairs of male and female Ss were divided randomly into experimental and control groups, and the experimental Ss were treated in 4 different groups: separate groups of males and females at each of two centers. A comparison between experimental and control Ss after 7 weeks of conditioning treatment for a 2-week period revealed no significant difference in number of wet nights between the female Ss of the 2 groups; the difference between the male Ss was significant. Experimental male Ss wet a total of 46 nights, control male Ss wet 108 nights ($P < .01$). In the follow-up, 4 of the 11 successes (3 males and 1 female) relapsed. Although the conditioning treatment was not very successful in this population, retreatment is recommended for better results. (10 refs.) - *A. C. Schenker.*

West Virginia University
Medical Center
Morgantown, West Virginia 26506

2639 **TRIAS, E. P.; LEVITSKY, L. L.; GROSSMAN, M. S.; & RAITI, S.** Comparison of HGH, oxandrolone and combined therapy in idiopathic hypopituitarism, Hand-Schuller-Christian and Prader-Willi syndromes. *Acta Paediatrica Scandinavica*, 62(1):108, 1973.

Growth acceleration from human growth hormone therapy (2 IU x 3 per week for 8 months) approximated that from oxandrolone treatment (0.25mg/kg/day for 8 months), with individual variation seen, whereas combined therapy did not significantly potentiate growth in a study of 6 idiopathic hypopituitary (1H) patients, 1 with Hand-Schuller-Christian (HSC) syndrome, and 1 with Prader-Willi (PW) syndrome. Human growth hormone in the case of the HSC patient consisted of 4 IU x 3 per week. Between each study period, neither hormone was administered for 4 months. During human growth hormone therapy, 5 of the 6 IH patients grew at 7.6 to 11.1 cm/year. With oxandrolone, 4 of the 6 IH patients and the PW patient grew at 6.5 to 10.2 cm/year. During combined therapy, all IH patients and the PW patient grew at 2 to 4 times the prestudy rate but not better than when either hormone was used alone. The HSC patient responded poorly to all 3 forms of therapy. Marked bone age acceleration was seen only in the PW patient. - *B. J. Grylack.*

2640 **SNYDERMAN, SELMA E.; SANSARICQ, CLAUDE; NORTON, PATRICIA; & PHANSALKAR, SADASHIV V.** The use of neomycin in the treatment of methylmalonic aciduria. *Pediatrics*, 50(6):925-927, 1972.

The oral administration of neomycin is reported effective in reducing the urinary excretion of methylmalonic acid in a child suffering from methylmalonic aciduria. The child was maintained on 0.8gm of protein/kg per day throughout the study. Two trials of oral neomycin at 250mg 4 times per day were made. There was a marked drop in urinary excretion of methylmalonic acid and in the plasma level of this metabolite during both trials of neomycin therapy. The average of 21 determinations of methylmalonic acid excretion during control periods was 2.08gm/day, whereas the average of 9 determinations during neomycin administration was 1.23gm/day. There was no effect on plasma amino acid levels. The results suggest that the gastrointestinal bacteria contribute significantly to either the propionate or methylmalonate pool. The use of a nonabsorbable oral antibiotic such as neomycin or kanamycin might be especially effective during periods of acute acidosis or when biochemical control is lost. (7 refs.) - *A. C. Schenker.*

New York University Medical
Center
New York, New York 10016

2641 Progress in behaviour therapy. *British Medical Journal*, 2(5812):478, 1972.

Much work has been devoted recently to con-

solidation of earlier advances in forms of behavior therapy now used widely. Wolpe's method of systemic desensitization is effective for phobic states, but some modification of treatment has been required, especially for patients with severe agoraphobia. Flooding (implosion) treatment, an alternative technique used by other psychiatrists, has produced results which are at least as good as those of desensitization. Aversion therapy, a third form of behavior therapy, is believed increasingly to depend on factors other than simple conditioning. Studies of these types of behavior therapy are raising important questions concerning the ways in which simple conditioning procedures are changed into the complex psychological and social changes used to measure psychiatric improvement. (8 refs.) - *B. J. Grylack.*

2642 **STIEHL, ADOLF; THALER, M. MICHAEL; & *ADMIRAND, WILLIAM H.** The effects of phenobarbital on bile salts and bilirubin in patients with intrahepatic and extrahepatic cholestasis. *New England Journal of Medicine*, 286(16):858-861, 1972.

The effect of phenobarbital on serum bile salts was investigated with 3 children with intrahepatic biliary atresia, idiopathic recurrent cholestasis, and extrahepatic biliary atresia, respectively. Bile salts were determined by gas-liquid chromatography. Serum concentrations of conjugated bile salts were decreased, and the fecal excretions of ^{131}I-Rose Bengal were increased during phenobarbital treatments in the 2 patients with intrahepatic cholestasis, a finding which suggested that stimulation of hepatic microsomal enzymes and enhancement of biliary secretion by drugs may occur independently. In the absence of extrahepatic biliary ducts, however, phenobarbital therapy produced no changes in clinical condition and did not alter serum concentrations of bile salts and bilirubin and fecal excretion of Rose Bengal. Serum concentrations of cholate were greater than concentrations of chenodeoxycholate in the 2 patients with intrahepatic cholestasis, while the reverse was true in the patient with extrahepatic biliary atresia. Whereas control of pruritus and reduction of jaundice in intrahepatic atresia appeared to require continuous phenobarbital therapy, short-term phenobarbital treatment seemed to be successful in ameliorating attacks of benign recurrent cholestasis. (27 refs.) - *B. J. Grylack.*

*University of California
San Francisco, California 94122

2643 **JOYCE, D. N.; & KENYON, V. G.** The use of diazepam and hydrallazine in the treatment of severe pre-eclampsia. *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 79(3):250-254, 1972.

Intravenous infusion of diazepam and hydralazine to 52 patients with severe preeclampsia in labor gave more favorable results than did administration of a lytic cocktail regime or rectal Avertin (tribromethanol) to a similar group of 30 patients. While the diazepam/hydrallazine regime produced a substantial and highly significant drop in mean maximum blood pressure, ($p < 0.001$) significant drop was seen with the lytic/Avertin regime. Neither the lytic nor the Avertin regime was wholly satisfactory for the treatment of severe preeclampsia, while the diazepam/hydrallazine regime controlled fits and blood pressure without producing any adverse reactions other than a tendency for the baby to become hypothermic. The diazepam/hydralazine regime was preferred uniformly by the medical and nursing staff because adequate sedation with these drugs still allowed patient cooperation. (5 refs.) - *B. J. Grylack.*

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Denmark Hill, London, S.E.5, England

2644 **ROGERS, STANFIELD.** Gene therapy for human genetic disease? *Science*, 178(4061):648-649, 1972. (Letter)

Reference is made to Friedmann and Robin's criticisms of therapy for two argininemics. It is submitted that the criteria set for gene therapy have been adequately met since the patients studied were investigated jointly by 3 groups of investigators from the genetic and biochemical aspects; the 3 children affected by the Shope virus are from the same family and deterioration of the disease followed the same course in the older children, although the baby has not yet undergone change. The virus was purified and testing for possible contamination proved negative; it has been studied for 40 years without having produced any harmful effects on any investigator, and massive doses in animals have shown no discernible effects except for a decrease in blood arginine concentration. The most direct evidence that the

arginase induced is virus information was published in 1971 and the complete data were not available in time to the authors for inclusion in their article. The Shope virus appears to be a rather ideal passenger virus to which desired genetic information may be added in the future for further efforts in gene therapy. (5 refs.) - *A. C. Schenker.*

Oak Ridge National
Laboratory
Oak Ridge, Tennessee 37830

2645 **NEUFELD, ELIZABETH F.; & SWEELEY, CHARLES C.** Gene therapy for human genetic disease? *Science*, 178(4061):648, 1972. (Letter)

Disagreement is voiced with Friedmann and Roblin's conclusion as to the negative response of storage diseases associated with lysosomal enzyme deficiencies to enzyme therapy. It is submitted that therapeutic replacement of deficient enzymes with plasma, leukocytes, or through transplanted kidneys has already shown promise in those systemic storage disorders in which the affected cells have marked pinocytic activity. The 2 cases cited by Friedmann and Roblin as refractory are not considered as representative. In one case, the disease selected for treatment, metachromatic leukodystrophy, may indeed be among those not responsive to enzyme replacement due to a disorder, as in other neurological diseases, wherein the blood-brain barrier may interfere with the circulating enzyme in reaching the brain cells. In the second case, the quantity of ceramide trihexosidase may have been too small for therapeutic benefits. (5 refs.) - *A. C. Schenker.*

National Institute of
Arthritis and Metabolic
Diseases
National Institutes of Health
Bethesda, Maryland 20014

2646 **FRIEDMANN, THEODORE; & ROBLIN, RICHARD.** Gene therapy for human genetic disease? *Science*, 178(4061):649, 1972.

In reply to the opinions expressed by Neufeld and by Rogers regarding gene therapy with enzyme preparations, certain relevant facts are stressed. Important problems exist in ensuring optimum uptake into cells, such as neurons, where the enzyme is critically needed. Further trials with purified enzyme preparations will be required to evaluate further the potential for enzyme therapy in lysosomal or other disorders. It is submitted that the use of Shope virus as a viral gene which codes for a virus-specific arginase is still questionable; Orth and his colleagues have shown that the Shope papilloma arginase has kinetic, molecular, and antigenic properties indentical to those of rabbit liver enzyme. Roger's comparison of live attenuated virus immunization with virus-mediated gene therapy is an unfair one; the Shope virus is oncogenic under some conditions and is capable of altering the patient's genetic pattern permanently. There have been no reports to date describing criteria for virus therapy in the medical or scientific journals. (6 refs.) - *A. C. Schenker.*

School of Medicine (Pediatrics)
University of California
San Diego, La Jolla 92037

2647 **ENTE, GERALD; LANNING, EDWARD W; CUKOR, PETER; & KLEIN, RICHARD M.** Chemical variables and new lamps in phototherapy. *Pediatrics Research*, 6(4):246-251, 1972.

Possible harmful effects of phototherapy (used in neonates) were investigated by *in vitro* studies designed to measure the effects of variations in concentrations of albumin and flux upon the photodecomposition of bilirubin; experimental lamps were also studied. A light exposure box was built to allow simultaneous exposure of 3 solutions by 3 different lamps; a Reeder thermopile was used to measure the total flux of each lamp. Absorption spectra were obtained with a Cary model no. 14 recording spectrophotometer. The efficiency of phototherapy was studied by varying flux levels while maintaining other variables constant. The effect of light flux is such that continuous exposure at the lowest practical level necessary to maintain the desired bilirubin concentration is most efficient. Further investigations are suggested to determine the exact *in vitro* decomposition products as well as other components which require standardization as to their toxicity reactions and interactions. (29 refs.) - *A. C. Schenker.*

Nassau County Medical Center
East Meadow, New York 11554

2648 **EISENBERG, LEON.** Symposium: behavior modification by drugs. III. The clinical use of stimulant drugs in children. *Pediatrics*, 49(5):709-715, 1972.

The use of stimulant drugs in children is discussed in terms of the physician's role in their prescription and what is known about their effects. It is incumbent upon the physician to consider those methods of treatment which may modify an otherwise potentially ominous course, in dealing with the overactive child. The most effective and the best documented are the stimulant drugs, dextroamphetamine and methylphenidate, agents which suppress overactivity and impulsivity and lengthen attention span. Appropriate strategy is to begin with a minimal dose (5mg dextroamphetamine or 10mg methylphenidate) to be given once each morning with breakfast; at 2-3 day intervals, if no improvement in behavior results, dosage should be increased in like increments. Once a child has responded, if a single dose is omitted he returns to baseline levels. The child is likely to require treatment for a prolonged period. There is no evidence of pharmacologic habituation. To terminate treatment, it is best to discontinue use over a long school vacation. Overactivity and distractibility can occur under circumstances in which drug use is contraindicated: intense anxiety due to a disorganized family life; hypoglycemia due to malnourishment; and in situations where classrooms are overcrowded or inadequate. There is no evidence of potential for adolescent drug abuse in children thus treated. Stimulant drugs, though only one element in a program of treatment, can be key factors in enabling the child to benefit from remedial education and parent counseling. (35 refs.) - *A. C. Schenker.*

Massachusetts General Hospital
Boston, Massachusetts 02114

2649 **GARDNER, JAMES M.** Selection of nonprofessionals for behavior modification programs. *American Journal of Mental Deficiency*, 76(6):680-685, 1972.

The results of 3 independent studies involving attendants and residents at 2 inst for the MR fail to support the hypothesis that new employees are better suited for inclusion in behavior modification training programs than are older employees. In the first study, no significant differences in attitude toward or knowledge of behavior modification were noted between experienced and inexperienced personnel. Additionally, experienced attendants in the second study were less likely to be sick or absent or to request transfer to another unit once they were included in an ongoing behavior modification project involving MR residents. In study #3, personality tests and evaluation of 7 behavior modification trainers working with 30 SMR and PMR Ss showed the most successful trainers to have the greater needs for achievement and affiliation. (7 refs.) - *N. Mize.*

Orient State Institute
Orient, Ohio 43146

2650 **BERNSTEIN, NORMAN R.; & RICE, JACK O.** Psychiatric consultation in a school for the retarded. *American Journal of Mental Deficiency*, 76(6):718-725, 1972.

Conventional methods of child psychiatric evaluation were employed to analyze the type and evolution of psychiatric disease among 303 inpatients and clinic patients at a school for the MR. A review of the consultations showed the eventual psychiatric diagnosis to reflect a wide range of mental disorders and to entail a similar wide variety of treatment modalities, including drugs, psychotherapy, and behavior modification. Psychiatrists involved in the training program became much more sensitive to the real problems experienced by parents of MR children and helped to open up new areas of research in personality development, learning difficulties, and environmental deprivation. Whether as consultant or therapist, the success of this program shows that the child psychiatrist in an inst setting can learn much from clinical work with the MR and can contribute substantially to the general upgrading of care on an interdisciplinary basis. (11 refs.) - *N. Mize.*

Walter E. Fernald State
School
Waverley, Mass. 02178

2651 **APOSHIAN, H. VASKEN.** The use of DNA for gene therapy—the need, experimental approach, and implications. *Perspectives in Biology and Medicine*, 14(1):98-108, 1970.

Adequate discussions of DNA therapy for human

disease must take account of its use as a therapeutic agent, model systems that can be used experimentally, and the moral and other implications of gene therapy. As a therapeutic agent, DNA offers hope for many congenital diseases; it can provide a normal or improved life for patients with nonfatal inherited diseases, such as inborn errors of metabolism. The administration of DNA for replacement therapy may be effected by delivering the missing gene to a mammalian cell deficient in this gene within the protective coat of a virus; such transduction with animal viruses has not as yet been accomplished. The experimental approach centers around the synthesis of a virus-like particle containing an animal host gene. It has been demonstrated that after certain types of infection with polyoma, a mouse virus, 10-20% of the new pseudoviruses formed contain fragments of host DNA. The DNA will function either as a cure or a treatment of somatic cell mutations, depending upon the physical integration of the pseudovirus DNA. Despite the general fears surrounding genetic research, genetic therapy should be considered openly and weighed against alternative drug therapy. (19 refs.) - *A. C. Schenker.*

University of Maryland
School of Medicine
Baltimore, Maryland 21201

2652 **ROOS, PHILIP.** Reconciling behavior modification procedures with the normalization principle. In: Wolfensberger, Wolf; Nirje, Bengt; Olshansky, Simon; Perske, Robert; & Roos, Philip. *The Principle of Normalization in Human Services.* Toronto, Canada, National Institute on Mental Retardation, 1972, Chapter 10, p. 136-148.

Behavior modification is based upon systematic application of the principles of learning, and is aimed at altering all forms of deviant behavior. The advantages of the therapy are chiefly practical; since it has been found workable in a wide range of deviant individuals and in a wide range of deviant behaviors, it can be applied by relatively untrained persons, results are achieved in a relatively short period of time, and it can be used in group application. Behavior modification contrasts with expressive counseling and psychotherapy in that it deals only with the present instead of with the past. It contrasts with the medical model of behavior in emphasizing behavioral symptoms and results rather than illness and healing. The criticism of behavior modification is that it is totally superficial and mechanistic, and that it is destructive of self-determination and human dignity. Some behavioral aspects of normalization are similar to behavioral modification techniques. The two methodologies are more similar than opposing both in ideology and practice, especially when considered as implications of process and goal or means and ends. Compatible use of both techniques may be found successful in achieving the objectives of normalization. - *C. Wares.*

National Association for Retarded
Children
Arlington, Texas

PROGRAMMATIC ASPECTS—Planning and legislative

2653 **WOLFENSBERGER, WOLF.** Miscellaneous other implementive strategies and mechanisms. In: Wolfensberger, Wolf; Nirje, Bengt; Olshansky, Simon; Perske, Robert; & Ross, Philip. *The Principle of Normalization in Human Services.* Toronto, Canada, National Institute on Mental Retardation, 1972, Chapter 19, p. 232-235.

Direct subsidy of handicapped individuals or their families is one method of enabling such persons to attain a relatively normative solution in their individual problems. Such subsidy in cases of borderline or transitional economic need might make the difference between expensive inst of an individual or a moderate cash outlay to ensure that he could remain in a home or normal environment. Expected abuse and chaos associated with programs of direct subsidy can be minimized by the establishment of appropriate administrative management procedures. Direct subsidy in combination with other new forms of assistance to handicapped persons may helpfully implement the principle of normalization in treatment of the handicapped. - *C. Wares.*

National Institute on Mental Retardation
Toronto, Canada

2654 **WOLFENSBERGER, WOLF.** *The Principle of Normalization in Human Services.* Downsview, Toronto, National Institute on Mental Retardation, York University Campus, 1972. Paperbound. $8.50, Canada; $9.50, elsewhere.

This 19-chapter paperback is the first book-length comprehensive treatment of the normalization principle. The first part consists of 5 chapters. Here the principle is defined as one that holds that services for the handicapped and socially devalued must be of such a nature as to allow them to live as normal and productive a life as possible, and its major implications are discussed. The second part, comprising 10 chapters, focuses on the application of the normalization principle to specific service areas. The last past of the book is concerned with safeguards for integrating services for the handicapped. - *B. J. Grylack.*

2655 **MCDOWALL, E. B.** Supporting services for the mentally handicapped. *British Medical Journal*, 2(5864):481, 1973. (Letter)

Referring to an article depicting the critical medical situation in the field of mental subnormality, it is submitted that the care of a mentally handicapped member of society should be the responsibility of a single body. The diverse needs of the MR person can then be unified within the compass of an entirely new national authority which would be accountable for the administration, planning, and operation of the whole service. There are no overwhelming difficulties in formulating an outline scheme for the work of such a new department. The national press and the public could perhaps add their support to a project which would constitute a major progressive reform. - *A. C. Schenker.*

2656 **RICHARDS, B. W.** Care of the mentally handicapped. *Lancet*, 1(7765):1390, 1972. (Letter)

An examination of statistical data concerning the number of inst mentally handicapped patients in England and Wales calls attention to a strong aging trend among the resident population, showing that the number of persons age 55 or older has more than doubled since 1954. This feature is attributable to an increased survivor rate and is of similar dimensions for both males and females. Current governmental planners involved in reorganizing residential services for the MR will need to incorporate this data on the changing type and age structure of the inst MR population as an important determinant of their eventual recommendations as to future needs in the area of care, staff, and facilities. (4 refs.) - *N. Mize.*

St. Lawrence's Hospital
Caterham, Surrey CR3 5YA

2657 **HAIGH, R. D.** Overpopulation and subnormality. *British Medical Journal*, 2(5807):235, 1972. (Letter)

With the transfer of care of mentally subnormal children from the Health Departments to Education Departments in April, 1971, ascertainment of the numbers of MR children is no longer accomplished. It appears that future provision for such persons will not be made successfully unless the number of children who remain a burden on society throughout their lives is known. The problem of overpopulation in Great Britain has many facets, among them the social deprivation and overfertility of most large families and the birth of a disproportionate number of MR children into these families. - *B. J. Grylack.*

PROGRAMMATIC ASPECTS—Community

2658 A right to love? *Lancet*, 1(7759):1057-1058, 1972. (Editorial)

A recent report on public and professional attitudes toward the social and sexual needs of handicapped people exposes the ignorance and myths which surround this subject in today's society. Classic psychoanalytical theory is invoked to help explain the persistence of these attitudes toward the mentally and physically handicapped

among the "normal" population, attitudes which have fostered the continued neglect of the handicapped individual's emotional and sexual needs. Since the problem is not primarily to be located in the specific attitudes of the hospital staff, but, instead, in the general attitudes of society at large, readers are cautioned against this too narrow interpretation of an otherwise extremely valuable report. (1 ref.) - *N. Mize.*

2659 **PERRIN, JANE C. S.; RUSCH, EDNA L.; PRAY, JANET L.; WRIGHT, GREGG F.; & BARTLETT, GLEN S.** Evaluation of a ten-year experience in a comprehensive care program for handicapped children. *Pediatrics*, 50(5):793-800, 1972.

In a retrospective evaluation of professional input and patient outcome during a 10-year period of operation of a comprehensive care program for handicapped children, charts of 75 patients, a 10% sample, were selected at random and reviewed to score patient and family functions at entry and exit from the program (patient variables) and to measure the number of clinic visits by physicians or the years of social worker involvement (program variables). Zero-order correlations were defined as a measure of mutual relationship among all the patient and program variables, and partial and multiple correlations were determined among selected subsets of variables. Despite some significant positive and negative correlations between patient and program variables, there was no significant zero-order correlation between the physician and social worker quantitative input determined and the improvement of patient or family function. The study suggested that an ongoing program evaluation could be incorporated economically into a service and training program of this type. (11 refs.) - *B. J. Grylack.*

Comprehensive Care Program
Cleveland Metropolitan General
Hospital
Cleveland, Ohio 44109

2660 **PRESIDENT's MENTAL RETARDATION COMMITTEE.** *Federal Programs for the Retarded: a Review and Evaluation*. Washington, D.C., U.S. Government Printing Office, June 1972, 271 p. $2.00.

Reports of 22 federal departments and agencies on their programs related to mental retardation are included. Departments reporting are Agriculture, Commerce, Defense, Health, Education, and Welfare, Housing and Urban Development, Interior, Justice, Labor, State, Transportation, and Treasury. Agencies reporting are ACTION, Appalachian Regional Commission, Civil Service Commission, General Services Administration, National Aeronautics and Space Administration, National Science Foundation, President's Council on Physical Fitness and Sports, Small Business Administration, U.S. Postal Service, and Veterans Administration. The typical form of report includes information on objectives, activities, level of funding, and future plans. - *C. Wares.*

2661 **COLBERT, JAMES N.; KALISH, RICHARD A.; & CHANG, POTTER.** Two psychological portals of entry for disadvantaged groups. *Rehabilitation Literature*, 34(7):194-203, 1973.

Employers and real estate agents were asked their feelings regarding a series of disadvantaged groups. Each respondent sample was administered a paired comparison form, which included 9 disadvantaged groups plus an additional tenth group representing the respondent, and a 9-point rating scale, including these same 10 groups plus 12 more disease, ethnic, professional, or social groups. The most marked implication from the overall results was that a generally consistent rank order of acceptance did exist for the groups rated in the study. It was shown that certain disadvantaged groups, drug addicts and student militants being the most prominent, not only meet with difficulty in gaining re-entry into the work community, but they encounter this difficulty consistently. The rank order of disadvantaged groups for housing acceptance differed from but was just as clear and as consistent as that for employment acceptance, with the self-reference group, realtors, and the elderly having the greatest acceptance and drug addicts, student militants, juvenile delinquents, and prison parolees, the least. MR ranked 15th in a 1 to 22 acceptability scale for housing. (2-item bibliog ; 5 refs.) - *B. J. Grylack.*

Los Angeles County Probation
Department
Los Angeles, California

2662 **RHYS-JONES, W. G.** Community services.

In: Griffiths, Margaret I., ed. *The Young Retarded Child: Medical Aspect of Care*. Baltimore, Maryland, Williams & Wilkins, 1973, Chapter 6, p. 62-70.

Community health, education, and social services should ideally be complementary in care of MR children. Excessive overlapping or unnecessary gaps in care can thus be avoided. The local health authority is concerned with early diagnosis, risk registers, assessment of handicaps, and management of child and family. It is essentially in the fourth category that educational and social services are involved as in domiciliary services, school and day care and sometimes residential care. Voluntary societies, both national and local, may assist strongly in these services. - *C. Wares.*

Salop County Council
Birmingham, England

2663 WOLFENSBERGER, WOLF. Typical programmatic and architectural implications of the normalization principle. In: Wolfensberger, Wolf; Nirje, Bengt; Olshansky, Simon; Perske, Robert; & Ross, Philip. *The Principle of Normalization in Human Services*. Toronto, Canada, National Institute on Mental Retardation, 1972, Chapter 4, p 30-52.

Programmatic and architectural implications of the normalization principle are essentially undifferentiated in application. The first dimension is concerned with the structure of interactions involving deviant or potentially deviant individuals directly, and the second is concerned with the way such persons are interpreted to others. These dimensions (interaction and interpretation) are present in normalizing actions on a personal level (involving individual human managers with individual/potentially deviant persons), on the level of primary and intermediate social systems (family, peer group, school, neighborhood, service agency), and on the societal level (educational system, legal system, social mores). Implications of these activities are manifest in both programmatic and architectural structures and objectives. The normalization principle in human services is empirically supported and validated. - *C. Wares.*

National Institute on Mental
Retardation
Toronto, Canada

2664 WOLFENSBERGER, WOLF. The principle of normalization as a human management model: evolution of a definition. In: Wolfensberger, Wolf; Nirje, Bengt; Olshansky, Simon; Perske, Robert; & Roos, Philip. *The Principle of Normalization in Human Services*. Toronto, Canada, National Institute on Mental Retardation, 1972, Chapter 3, p. 26-29.

The principle of normalization has become a model for human management and services. The principle has been variously defined and evolved. A usefully broad definition of the principle is "utilization of means which are as culturally normative as possible," to establish and/or maintain culturally normative personal behaviors and characteristics. The normalization principle is thus culture-specific and implies both process and goal. According to the ideologies of a specific society, normalization may be either offered or imposed upon individuals who are culturally deviant. - *C. Wares.*

National Institute on Mental Retardation
Toronto, Canada

2665 WOLFENSBERGER, WOLF. Societal integration as a corollary of normalization. In: Wolfensberger, Wolf; Nirje, Bengt; Olshansky, Simon; Perske, Robert; & Roos, Philip. *The Principle of Normalization in Human Services*. Toronto, Canada, National Institute on Mental Retardation, 1972, Chapter 5, p. 44-54.

Societal integration of deviants may occur on physical/social levels. Physical integration involves location, physical context, access, size, or dispersal of deviant persons and associated facilities with normal persons and facilities. Social integration involves the specific features of normalizing programs; labeling of programs, persons, and facilities associated with deviants; and programs for building useful perceptions in the society concerning deviancy and normalcy. Integration at both levels is desirable for achieving normalization. Current integrative opportunities are available in educational programs, industry-integrated work stations, residences for special-need groups, medical services, recreational sites and facilities, and even religious congregations. Caution in integration with the objective of effective normalization must

be exercised in order to avoid reisolation of deviant persons. Integration is one of the most significant corollaries of normalization. - *C. Wares.*

National Institute on Mental Retardation
Toronto, Canada

2666 ANTONELLO, BARBARA L. Problems of enforcing the rights of the mentally retarded. *Notre Dame Lawyer*, 48:1313-1333, 1973.

The basis for recognizing the legal rights of the MR and the commensurate problems which arise from judicial intervention are outlined. The right to a free, publicly supported education for MR individuals, insofar as it applies to jurisdiction, is illustrated by a case which came to court; the court ruled that inaction in this matter would result in the court's appointing a special master to implement the judgment in favor of the defendants, should such education be denied to the MR. Another result of litigation was in the matter of adequate habilitation for such cases; in this case the lack of funds was given as the main reason for inadequate treatment. The ruling in such cases was that such funding was the responsibility of the state legislature. While in the educational area a direct financing order against a state legislature is inappropriate, such an order could be directed against the department of education. In the case of adequate habilitation, the state must find the funds for this by releasing surplus funds or by other means to bring the inst within the constitutionally required minimum standards. It is predictable that once the public is made aware of the substandard situation in the habilitation of the MR, it would force the state legislators to appropriate the necessary funds. (122 refs.) - *A. C. Schenker.*

2667 GREEN, FREDERICK C. The new National Center for Child Advocacy. *Clinical Pediatrics*, 11(1):609-610, 1972.

A National Center for Child Advocacy is being established by the Office of Child Development in the Dept of HEW. It will essentially consist of 3 divisions: a Children's Concern Center, to which persons throughout the country can turn for information regarding any aspect of child or youth development; an Information Secretariat, which will function as a clearinghouse for news of current developments in the related federal programs; and a Division of Vulnerable Children, which will be responsible for the well-being of children in insts and foster homes, for solving problems in child abuse, and for various parent education programs. All units will be staffed by trained professionals who have a genuine interest in children and who will speak out as advocates on behalf of their well-being. - *N. Mize.*

Office of Child Development, DHEW
Washington, D.C. 20013

2668 WALLACE, HELEN M. Present status and future directions for the care of handicapped children in large cities of the United States. *Clinical Pediatrics*, 11(1):4-7, January 1972.

Recently experienced difficulties in trying to elicit and compile statistical data on the care of handicapped children in large American cities emphasize the urgent need to decentralize and regionalize the existing State Crippled Children's Programs. Of the 150 cities initially surveyed, only 84 responded. Overall, the information provided was meager in response to queries about the local availability of services for handicapped children, their annual case loads, and the average waiting periods and waiting lists for both official and voluntary agencies. Since most of the services for handicapped children need to be delivered locally, this information is essential for planning and administration needs. A program of decentralization, such as that recommended, should aim to make this data readily accessible - *N. Mize.*

University of California School of Public Health
Berkeley, California

2669 Handicapped children and family stress. *British Medical Journal*, 1(5796):329-330, 1972. (Editorial)

A doctor should inform the patient's family of incurable conditions such as Down's syndrome or spina bifida. Then hospital clinics should give coordinated care and provide liaison with community services such as schools, transportation to hospital, temporary care, and assistance to parents. (5 refs.) - *V. J. Goldberg.*

2670 JONES, D. C. Confinement of subnormal offenders. *British Medical Journal*, 3(5834):231-232, 1972. (Letter)

In order to be consistent with the trend towards normalization in the area of MR, MR individuals who commit offenses should pay the penalty in accordance with the law. With few exceptions, no cure has been effected for such cases. An effort must be made to determine and establish proper facilities to deal with these patients that will be neither too strict nor too lenient. - *B. J. Grylack.*

Hensol Hospital, near Pontyclum
Glamorgan, Wales

2671 WOLFENSBERGER, WOLF. The role of ideology in shaping human management models. In: Wolfensberger, Wolf; Nirje, Bengt; Olshansky, Simon; Perske, Robert; & Roos, Philip. *The Principle of Normalization in Human Services*. Toronto, Canada, National Institute on Mental Retardation, 1972, Chapter 1, p. 6-10.

Man's behavior is largely determined by ideologies, such as religions, political systems, philosophies of life, and so on. Ideologies in human management professions are also behaviorally affective, and may be beneficial or harmful to the clients of such systems. A hereditary theory of MR may lead to treatment nihilism as opposed to an environmental theory that favors treatment activism. Ideologies transcending empiricism but not inconsistent with it are more productive in human services than those which are directly empirical, since the former allows for future development of treatment methodology and associated services, while the latter deals only with current observables. Unconscious ideologies may prove to be those which are the most harmful in rendering human services, since they offer contradictions in philosophy and practice. Man's patterns of response to devalued groups of fellow men demonstrate such ideologies. - *C. Wares.*

National Institute on Mental Retardation
Toronto, Canada

2672 WOLFENSBERGER, WOLF. The concept of deviancy in human management. In: Wolfensberger, Wolf; Nirje, Bengt; Olshansky, Simon; Perske, Robert; & Ross, Philip. *The Principle of Normalization in Human Services*. Toronto, Canada, National Institute on Mental Retardation, 1972, Chapter 2, p. 12-25.

The social definition of deviancy is an important concept in human services. A person is said to be deviant if he is significantly different from others, and if this difference is negatively valued. Deviancy is thus in the eye of the beholder rather than being a concrete entity. Deviants by society's definition include MR, handicapped or disfigured, aged, ill, unattractive, minority, and talented persons, as well as delinquent and legal offenders. The generality of attitudes toward deviancy is noticeable in patterns of attitude response to different types of deviants, such as the Puritan ethic which equates goodness with beauty and normalcy. Many insts for services to deviants reflect this general response, grouping MRs with criminals, for instance. Major historic roles imposed on deviant persons are: a subhuman organism, a menace, an unspeakable object of dread, an object of pity, a holy innocent, a diseased organism, an object of ridicule, and an eternal child. Societal management of deviancy has consisted of destruction or segregation of deviant individuals and reversal or prevention of the deviant condition. - *C. Wares.*

2673 WOLFENSBERGER, WOLF. Normalization via agency performance assessment and differential funding. In: Wolfensberger, Wolf; Nirje, Bengt; Olshansky, Simon; Perske, Robert; & Roos, Philip. *The Principle of Normalization in Human Services*. Toronto, Canada, National Institute on Mental Retardation, 1972, Chapter 18, p. 222-231.

Accountability is necessary in human services, and the means are available for such assessment of performance. One such accounting scheme, Program Analysis of Service Systems (PASS), includes rating elements such as ideology, administration, and funding. The analysis system was designed to assess quantitatively and compare the quality of human services, incorporate normalization principles as major criteria of program evaluation, assure reasonable reliability across raters, and provide adaptability to various service programs. PASS may be used to establish standards for normalizing human management agency performance, provide objective means of assessment, provide a rational means for allocating funds on a

competitive basis, and function as a teaching tool in disseminating the normalization principle. A system called FUNDET (funding determination) may be used in conjunction with PASS to make differential funding decisions for service projects which are of equal PASS quality. - *C. Wares.*

National Institute on Mental Retardation
Toronto, Canada

2674 **WOLFENSBERGER, WOLF.** Normalization via citizen advocacy. In: Wolfensberger, Wolf; Nirje, Bengt; Olshansky, Simon; Perske, Robert; & Roos, Philip. *The Principle of Normalization in Human Services.* Toronto, Canada, National Institute on Mental Retardation, 1972, Chapter 17, p. 216-221.

Citizen advocacy of normalization of adult MRs implies a commitment to noninst of such adults whenever possible. Alternatives to inst include foster parents, adoptive parents, citizen-guardians, and citizen-friends for the dependent handicapped. The concept of normalizing protective services has suffered from numerous shortcomings such as agency rigidity in allowance of such services, but a strong advocacy of normalizing protective services can effectively deal with such problems. Pioneer advocacy service systems were established in Nebraska in 1969-70, and may serve as models for further development of the program. - *C. Wares.*

National Institute on Mental Retardation
Toronto, Canada

2675 **WOLFENSBERGER, WOLF.** Some safeguards for integrative services. In: Wolfensberger, Wolf; Nirje, Bengt; Olshansky, Simon; Perske, Robert; & Roos, Philip. *The Principle of Normalization in Human Services.* Toronto, Canada, National Institute on Mental Retardation, 1972, Chapter 16, p. 208-214.

Services to special groups of handicapped persons are preferably contracted and initiated from generic agencies rather than from specialized agencies. A coordinated service system may be developed by opening generic agencies to special clients, orientation of generic workers toward special conditions, redefinition of functions of special services and criteria for utilization, placement of specialists into generic services, and development of coordinating mechanisms within communities. Administrative safeguards for such integrative services might include: vesting major responsibility in a specialty point, regulatory control of services, agreement on program quality, funding related to performance assessement, consumer-client representation, citizen advocacy, watchdog committees, placement of specialists into generic agencies, provision of specialized consultants, and supportive specialty services. Integration of services for special groups with normal services is an important step toward implementation of the normalization principle in human services. - *C. Wares.*

National Institute on Mental Retardation
Toronto, Canada

2676 **INTERNATIONAL LEAGUE OF SOCIETIES FOR THE MENTALLY HANDICAPPED.** *Symposium on the Development and Operation of National Societies for the Mentally Retarded: Conclusions. Lisbon, 20-22 March, 1972.* Brussels, Belgium, International League of Societies for the Mentally Handicapped, 1972, 39 p.

The fifth Symposium on the Development and Operation of National Societies for the Mentally Retarded, held in Lisbon, Portugal, 20-22 March 1972, reached conclusions in 4 areas: objectives, means of action, organizational structure, and stages of development. Objectives determined included integration and normalization of the MR in practical terms through participation of the community as it evolves to a position of responsibility in direct services to MR persons. Means of action are concerned with available personnel, design and provision of appropriate program(s), and funding. Organizational structure was determined at three levels and functions: local, primary contact and direct services; regional, information and coordination of local services; and national, encouragement and assistance to services, promotion of understanding and meaningful research, and development of professional personnel. Stages of development are visualized as meetings of parents and creation of specific facilities, cooperation between groups of parents, and realistic recognition and assessment of the problem of

retardation and concomitant activity by statutory authority. - *C. Wares.*

International League of Societies
for the Mentally Handicapped
Brussels, Belgium

2677 Mental Health Law Project. *Basic rights of the mentally handicapped: right to treatment, right to compensation for institution-maintaining labor, right to education.* Washington, D.C., Mental Health Law Project, 1973, 123 p. Mimeo. Paperbound, $1.25.

This booklet is designed as an introduction for the general reader, administrators, and mental health professionals and paraprofessionals to some of the basic legal rights of the mentally ill and MRs. Some of the prototype legal cases intended to aid the mentally ill in achieving their rights are described, and various court-ordered standards and provisions ensuing from this litigation are appended. - *B. J. Grylack.*

1751 N Street, N. W.
Washington, D. C. 20036

PROGRAMMATIC ASPECTS—Residential

2678 **SIMON, G. B.** Services: Hospital provision. In: Griffiths, Margaret I., ed. *The Young Retarded Child: Medical Aspects of Care.* Baltimore, Maryland, Williams & Wilkins, 1973, Chapter 7, p. 71-80.

The function of the hospital in serving the MR child is dual: initial treatment for every handicapped child and additional or long-term treatment for some of these children. The initial treatment includes early detection and assessment, and specific treatment and management aimed at bringing the child to his full potential in the community. Long-term treatment is necessary for the severely physically handicapped and/or frail child, the overactive and disturbed child, the inactive and MR child, and those needing specialized treatment and training of some duration. Some standards for hospital long-term facilities and staffing need to be set. Some important constituents in the long-term facility are: integration/cooperation among specialized staff members and consultants, such as pediatrics, subnormal specialists, and local medical personnel; child care facilities; specialized units for assessment and treatments; integral or relevantly located care units; primary education facilities with a fully developed program of educational aims and policy, teaching techniques, and specialized materials. Hospital care for the MR also includes the special needs and objectives of outpatient care and guidance. The hospital environment is an important factor in the effectiveness of such care, both medical and therapeutic. - *C. Wares.*

Institute of Subnormality
University of Birmingham
Birmingham, England

2679 **PRIMROSE, D. A.** Confinement of subnormal offenders. *British Medical Journal*, 3(5837):425, 1972. (Letter)

The therapeutic community of a mental subnormality hospital, which removes temptations and limits the chances for misbehavior, can often provide an acceptable mode of living for mentally subnormal offenders, most of whom cannot be cured. Once they have become settled within a specific unit designed for them within the large subnormality hospital, many of them are able to move on to the more open facilities provided by the hospital. - *B. J. Grylack.*

Royal Scottish National Hospital
Larbert Stirlingshire, Scotland

2680 **SHAPIRO, A.** Care of the mentally handicapped. *British Medical Journal*, 2(5809):352, 1972. (Letter)

Improvements in hospitals for the mentally handicapped must be made according to a schedule compatible with the everyday needs of patients and of the clinicians who care for them. If all improvements in the quality of hospital services are stopped before adequate alternative provisions are made, the hospitals will not be able to meet their commitments to the community they serve, and the present hospital population will be condemned to continue life under unacceptable conditions. - *B. J. Grylack.*

Harperbury Hospital
St. Albans, Herts, England

2681 **WOLFENSBERGER, WOLF.** Additional architectural-environmental implications of the normalization principle. In: Wolfensberger, Wolf; Nirje, Bengt; Olshansky, Simon; Perske, Robert; & Roos, Philip. *The Principle of Normalization in Human Services*. Toronto, Canada, National Institute on Mental Retardation, 1972, Chapter 6, p. 56-77.

As human services are generally located in buildings and these buildings affect the way in which services can be or are delivered, how they are publicly perceived, how service recipients are publicly and self-perceived, the architectural-environmental implications of the normalization principle are demonstrably important. A building may be a monument, a public relations medium, or a service medium. The focus of convenience of a building may be according to the architect, the community, the staff, or the client-user. The architectural implications of certain role perceptions of the client-users of buildings may be reinforced or diminished by a building, affecting both public and self-perceptions such as the client as subhuman (right to privacy, property, communication, individuality), as a menace to society, as an object of pity, as sick, as a burden of charity, as an object of ridicule, as an eternal child, or as a holy innocent. The implications of the normalization principle with reference to internal design involve such aspects of normalization as enrichment or behavioral modification. Current building codes often do not coincide with such implications and objectives, and should be revised where possible. Environmental design of human service facilities in terms of the objectives of such services is a neglected field, and one of great importance to the concept of normalization. - *C. Wares.*

National Institute on Mental
Retardation
Toronto, Canada

2682 **WOLFENSBERGER, WOLF.** Additional implications of the normalization principle to residential services. In: Wolfensberger, Wolf; Nirje, Bengt; Olshansky, Simon; Perske, Robert; & Roos, Philip. *The Principle of Normalization in Human Services*. Toronto, Canada, National Institute on Mental Retardation, 1972, Chapter 7, p. 78-92.

Residential components are common within human management systems. They are major components in the areas of MR, mental disorder, geriatrics, and correction. The implications of the normalization principle for such residences and the services available therein are manifest in 5 areas: integration, smallness, separation of domiciliary function, specialization, and continuity. Special considerations relating to normalization should be differentiated according to the clients of such residences, whether children, adults, aged, or general population. Individual placements in residences for family boarding or foster/adoptive environments should also correspond to the normalization principle. The manpower objection to dispersal of services according to the normalization principle can be met with the provision of back-up personnel such as consultants, itinerant counselors, recreation specialists, and miscellaneous volunteer personnel. The efficacy of small, specialized residences as a substitute for inst residences is complementary to the normalization principle. - *C. Wares.*

National Institute on Mental
Retardation
Toronto, Canada

2683 **SHAPIRO, ALEXANDER.** Care of the mentally handicapped. *British Medical Journal*, 1(5795):308-309, 1972. (Letter)

Two letters dealing with some fundamental points in services for the mentally handicapped by the Department of Health and Social Security are reviewed. One point concerns the care of the subnormal child at home, wherein it is assumed that the cost of keeping a handicapped child in the community is less expensive than placing the child in a hospital. This is not true; the cost is twice as high to maintain a child in the community, at least in the London Metropolitan area. Another point deals with deterioration on discharge; patients do break down if they are not given skilled nursing care; the patients cannot be cared for properly in hostels, even if they accepted such handicapped persons. The needs of the adult handicapped person seem to be ignored by the services. It is unfortunate that the Department is committed to community care to the exclusion of improvement in the quality of care in the hospital. There is another danger, that of the care of the mentally handicapped being divided between a number of specialists to whom the care of these people will

represent a fringe interest. (2 refs.) - *A. C. Schenker.*

Harperbury Hospital
Nr. St. Albans, Herts
England

2684 EYMAN, R. K.; O'CONNOR, G.; TARJAN, G.; & JUSTICE, R. S. Factors determining residential placement of mentally retarded children. *American Journal of Mental Deficiency*, 76(6):692-698, 1972.

In an examination of factors influencing the likelihood that specific MR children will be inst by their families, it was found that the 5 most significant variables distinguishing between a high and low probability of inst represent characteristics of the patients themselves. Of the family-based factors considered, only difficulties in supervision and care and health problems discriminate. None, however, show the same level of significance as the 5 patient characteristics. Of 143 children identified in the study as MR, 113 required no residential care during the course of the 5-year study and follow-up period. A profile of those admitted to inst during this time, as compared to those who remained at home with their families and utilized outpatient community resources, shows the inst group generally to be Anglo and younger, to have IQ s of less than 53, more physical disabilities, and more adaptive behavior failures. (41 refs.) - *N. Mize.*

Pacific State Hospital
Pomona, California 91768

2685 Staffing our asylums. *British Medical Journal*, 1(5799):523-524, 1972. (Editorial)

Whittingham Mental Hospital has 2,000 patients, of whom 85% have been there 2 or more yr. Some provision should be made for the mentally ill MR (60,000 inst and 100,000 receiving community services), the aged (37,000 within NHS, 35,000 in mental hospitals, and 50,000 in private and local authority nursing homes), and for the unknown number of patients who remain at home because their families do not want to send them away to an isolated, overcrowded, antiquated asylum. It is difficult to recruit staff to work in geographically isolated, long-stay units. The acute-care units of these hospitals should not be removed to the community hospitals until some provision is made for the custodial care of the long-term patient in the community. (5 refs.) - *V. J. Goldberg.*

2686 PRIMROSE, DAVID A. Care of the mentally handicapped. *British Medical Journal*, 1(5799):568, 1972. (Letter).

Hostels cost more than large hospitals for the MR and have fewer training and recreation facilities. Comparison between countries is not valid, because the high-grade MR (IQ 70-84) offender may be treated by the health care system or by the penal system. Existing residential facilities should perhaps be improved rather than abandoned. - *V. J. Goldberg.*

Royal Scottish National Hospital
Larbert, Stirling
Scotland

2687 KUSHLICK, ALBERT. Care of the mentally handicapped. *British Medical Journal*, 1(5801):686, 1972. (Letter)

Shapiro's letter (29 Jan. 1972, p. 308) was critical of experimental units with high staff ratios because they were too expensive. The ratio at Brookland Hospital is 1 staff member to 8 children, and since many patients are severely behavior-disturbed children requiring custodial care, the ratio is not generous. The lack of educational, social, or vocational facilities is due to lack of funds and the attitude that these services are of no benefit for these patients. The new proposals for treatment-oriented hospitals may result in some successes which might generate more optimism. (5 refs.) - *V. J. Goldberg.*

2688 RICHARDS, B. W. Care of the mentally handicapped. *Lancet*, 2(7785):1029-1030, 1972. (Letter)

Accommodations to be provided for the MR in England will number 68 places per 100,000 population, a figure which includes the residential units to be made available for hospital-type cases in independent units or units in existing hospitals. Most elderly patients, among whom the incidence of severe subnormality is increasing, are ambulatory, continent, and able to feed and dress themselves. In view of the desires of many elderly patients not to be moved, it is assumed that the transfer of patients from hospital to local

authority accommodation will be selective with regard to age groups. (3 refs.) - *B. J. Grylack.*

St. Lawrence's Hospital
Caterham, Surrey CR3 5YA, England

2689 **BLEADEN, F. A.; & PRICE, J. H.** Future of mental health services. *British Medical Journal*, 1(5805):624-625, 1972.

It is unrealistic to abolish mental hospitals because these institutions are needed for care of chronically disturbed patients who cannot be suitably cared for in district general hospitals, acute care units, or in local authority hostels. The mentally ill MR (IQ 50 to 80) are not accepted at hospitals for MR and do not benefit from psychiatric therapy. Units in small cities would be too small to provide many services and it may be more expensive to staff a small unit. The psychiatric nursing staff may not receive full cooperation from the general nursing staff. - *V. J. Goldberg.*

St. John's Hospital
Lincoln, England

PROGRAMMATIC ASPECTS—Recreational

2690 Committee on Children with Handicaps: Day care for handicapped children. *Pediatrics*, 51(5):948, 1973. (Editorial)

The Committee on Children with Handicaps has issued a statement on the need for special day care programs for handicapped children. Whenever possible, such children should be integrated into the same groups and programs as other children; no children should be isolated, segregated, or excluded. Even when day care programs are available for all children, the need for special programs for the handicapped will be great; these can be provided as a supplement to the day care program, for example, physical therapy and speech training for a child with cerebral palsy. Some children with severe handicaps such as deafness, blindness, or severe MR should have programs where they are in close proximity to those for normal children. Training programs for personnel to work with handicapped children should be increased. - *A. C. Schenker.*

FAMILY

2691 **BOONE, DONALD R.; & HARTMAN, B. H.** The benevolent over-reaction. *Clinical Pediatrics*, 11(5):268-271, 1972.

"Benevolent Over-Reaction" (BOR) a common cluster of parental actions which typically includes overprotection, overindulgence, and permissiveness toward a handicapped child, should be anticipated by the physician. Early identification of this malignant relationship and the immediate initiation of constructive counseling with parents is particularly important if the unfortunate consequences -- including emotional disturbance, MR, and a generalized inability to cooperate on the part of the child -- are to be prevented. In many cases prophylactic counseling at the time when the child's handicap is first diagnosed may be appropriate, since all too often the insidious effects of BOR are identified only after an irreversible pattern has been established. Most frequently, pediatricians, general practitioners, and nurses—particularly public health nurses and nurse practitioners—will be best situated to make the early identification of such handicapping parental attitudes. - *N. Mize.*

Clinic of Western North Carolina
Asheville, N.C. 28801

2692 **HOLDAWAY, DAVID.** Educating the handicapped child and his parents. *Clinical Pediatrics*, 11(2):63-64, February 1972.

In the just excitement surrounding recent medical advances in the treatment and diagnosis of handicapped children, the very real emotional and educational needs which accompany this increased survival time are often overlooked. To maximize the full potential of the handicapped child's situation the problems of both the child and his family must be specifically considered. For the child preschool teaching facilities are becoming

generally recognized as essential to the improvement of later educational, social, and vocational achievement. With the parents, the very real emotional problems entailed in the acceptance and rearing of a handicapped child must be confronted directly by the physician. Guidance and support to the parents and siblings of a handicapped child are vital to the affected child's development as a human being (3 refs.) - *N. Mize.*

University of Otago Medical
School
Dunedin, New Zealand

2693 **NUGENT, JOHN.** Influences on child development. *Lancet*, 2(7787):1140, 1972. (Letter)

The influences on the development of children are wider than the editorial (*Lancet*, Nov 4, 1972, p. 960) indicates. The predictive value of the parents' social status requires the inclusion of data concerning family history, the history of each family member, and an account of the present and past status of the family within the neighborhood. A knowledge of the child's and parents' personalities would be useful in predicting periods of stress and deprivation. One of the difficulties in understanding family behavior is establishing the true focus of disturbance or deprivation (who may not be the most disturbed family member). The problems presented by the disturbed or deprived child are complex and are best handled by a multidisciplinary team which tries to assess all the influences exerted on the child and to meet his individual needs. - *V. J. Goldberg.*

Merrified Children's Unit
Norton Fitzwarre, Taunton
Somerset, England

2694 **BENTOVIM, ARNON.** Emotional disturbances of handicapped pre-school children and their families -- attitudes to the child. *British Medical Journal*, 3(5826):579-581, 1972.

The birth and development of a handicapped child can be accompanied by potential parental crises. The parental role is important even before birth, for problems arising prior to and during pregnancy may have an effect on the quality of the initial maternal state and subsequent mothering ability. Unless the birth of the handicapped child is handled with considerable skill, long-term failures in holding, adaptation, and attachment to the child may occur. The impact may be less if a handicap is diagnosed through later symptoms or regular observations of the infant in the clinic, but problems may persist from infancy if there is a failure to resolve the early crisis adequately. At each state of the child's development the parents may experience a fresh sense of loss; a precarious emotional balance may become shattered, and rage, depression, and child abuse may be the result. The family, and particularly the mother, should be supported by professionals and taught the necessary skills to cope, and comprehensive assessment and aid from the health service team should be available. (11 refs.) - *B. J. Grylack.*

Hospital for Sick Children
London, England

PERSONNEL

2695 **WOLFENSBERGER, WOLF.** Implications in the field of mental health. In: Wolfensberger, Wolf; Nirje, Bengt; Olshanky, Simon; Perske, Robert; & Ross, Philip. *The Principle of Normalization in Human Services*. Toronto, Canada, National Institute on Mental Retardation, 1972, Chapter 8, p 94-120.

The most extensive elaboration of the normalization principle has occurred in the area of MR, and the implications of the principle in this application are relevant for the entire mental health field. The field of mental health is at the present time in turmoil, caught in a conflict between traditionalism and external challenges to the viability of services. Public perception of the turmoil amounts to apathetic rejection of the methods utilized in mental health, with related sociopolitical repercussions. The prevailing ideology in mental health of treatment for intrapsychic and family dynamics is inadequate to meet the challenge of social and economic factors in mental health. Normalization is a better ideological alternative in terms of social reality. Normalization in mental health could enhance and strengthen the conceptualization of

the client's role and of comprehensive services, while dramatically affecting the structure of mental health residential services for both children's and adults' programs. Manpower implications of the normalization principle in mental health would be the encouragement and progressive use of disciplinary services in place of individual therapists, the normalization of deviant groups and individuals in juxtaposition, and improved career modeling. Normalization in mental health would presuppose the development of more systematic management according to societal needs, such as dealing with group-social factors before crises occur. - *C. Wares.*

National Institute on Mental
Retardation
Toronto, Canada

2696 BORGSTEDT, AGNETA D. The pediatrician as ombudsman for the handicapped child. *Pediatrics*, 51(6):1107, 1973. (Letter)

Dr. Battle is to be congratulated for her discussion of the role of the pediatrician as ombudsman in the health care of the handicapped child. She expresses well the opinions of many pediatricians in the Rochester School of Medicine and Dentistry. The Committee for the Handicapped in the Academy of Pediatrics is indeed trying to serve as ombudsman between the handicapped child and his or her family and the community. (1 ref.) - *A. C. Schenker.*

University of Rochester
School of Medicine and Dentistry
Rochester, New York 14642

2697 BOWIE, E. MARY. Services: The family doctor. In: Griffiths, Margaret I., ed. *The Young Retarded Child: Medical Aspects of Care*. Baltimore, Maryland, Williams & Wilkins, 1973, Chapter 5, p. 50-61.

The family doctor's role in care of the young MR child is important. The doctor's role includes detection of MR, assessment and referral, general care of the family, including informing them of the MR and recommended treatment, and physical care of the child. Direct care of the child will include dental care; feeding difficulties management; treatment of gastrointestinal disorders, respiratory tract infections, and convulsions; dealing with sleep disorders; immunization schedules; provision and training in the use of prosthetics or appliances; and other medical procedures as required with a normal child. Family counseling may also be necessary in the case of genetic problems. The doctor's knowledge of and cooperation with other sociomedical disciplines and organizations are also helpful adjuncts to his treatment regime. The doctor's role in care of MR children is thus seen to be primary. - *C. Wares.*

Mid-Worcestershire Hospital
Management Committee
Worcestershire, England

2698 BATTLE, CONSTANCE U. The role of the pediatrician as ombudsman in the health care of the young handicapped child. *Pediatrics*, 50(6):916-922, 1972.

It is the logical role of the pediatrician to assume responsibility and leadership of the team in dealing with the young handicapped child. Examples of congenital malformation, in particular craniofacial malformations, illustrate a neglected aspect of diagnosis and treatment. The responsibility of the pediatric ombudsman is visualized as the reviewing of all aspects of the child's functioning with specialists caring for him, with his family, and with school and community. The story of Lee, a child with acrocephalosyndactylism or Apert's syndrome, illustrates the suffering of the mother who was not shown the child; through ignorance and poor judgment, the physician aggravated rather than eased the mother's anxiety. When Lee was 5 months old, his mother discovered that she was again pregnant and more anxiety ensued. The mother had feelings of guilt regarding her deformed child and was afraid of repeating the experience. The role of the physician in such a situation is important to help not only the child but also his family and to learn all he can from the specialists so that he may assume direct treatment of the child. (25 refs.) - *A. C. Schenker.*

Center for Craniofacial Anomalies
Oak Park, Illinois 60302

2699 SPENCER, D. A. Consultants in mental handicap. *British Medical Journal*, 3(5837):425, 1972. (Letter)

At the present time, 125 consultants specializing in mental handicap in England and Wales are responsible for approximately 59,000 hospitalized mental inpatients in addition to their many other commitments. More consultants will be needed to achieve the more ideal ratio of 1 consultant to 200 to 250 inpatients and to meet the needs of extended community provision, but there is difficulty in filling consultant posts in this specialty. The medical profession is failing to attain the standard it should reach in the care of the mentally handicapped. (4 refs.) - *B. J. Grylack.*

Meanwood Park Hospital
Leeds, England

2700 **ENG, GLORIA D.** The physician, education and the handicapped child. *Clinical Proceedings, Children's Hospital National Medical Center*, 28(4):83-84, 1972. (Editorial)

As an observer of the catastrophic effects of a handicapped child on a family psychically, socially, and economically, the physician cannot confine himself to diagnosing the handicapping condition but must counsel and support the family in realistic goal planning and become involved in the search for appropriate educational facilities. The model preschool and early education projects for handicapped children authorized by the federal government represent a significant improvement over most existing facilities. However, their implementation depends upon proper leadership and critical evaluation on the part of physicians, educators, and mental health specialists, as well as the community. (2 refs.)- *B. J. Grylack.*

AUTHOR INDEX

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